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Faculty will disclose that the use in question is not currently approved by the FDA per the product labeling or marketing.Full disclosure of faculty relationships will be made prior to the activity. Navbar Submission Request History As a library, NLM provides access to scientific literature. Inclusion in an NLM database does not imply endorsement of, or agreement with, the contents by NLM or the National Institutes of Health. Learn more: PMC Disclaimer | PMC Copyright Notice The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 33 National Cancer Institute designated Comprehensive Cancer Centers dedicated to patient care, research, and education. The NCCN is best known for the establishment of tumor-specific clinical practice guidelines. These are based on the evaluation of evidence and formulation of recommendations by a panel of experts for each type of cancer. The impact has been far-reaching: in 2022, the CNS Guidelines were downloaded 177 296 times, including 25 944 from sites outside the United States. The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers1 are formed by the efforts of a committee of 34 members compromised of 12 neurologists, 7 radiation oncologists, 5 neurosurgeons, 7 medical oncologists, 1 neuropathologist, and 1 patient advocate. Each year, the Guidelines are reviewed and updated by the committee members. During the review period, member institutions, industry representatives, and individuals outside the NCCN can submit comments, which are then collated and discussed at the annual committee meeting held at the NCCN Headquarters in Plymouth Meeting, PA. The data supporting these comments are analyzed by the committee to decide whether to add to or revise the guideline algorithms using the NCCN Categories of Evidence (1, 2A, 2B, 3) as shown in Table 1. The committee votes on assigning category recommendations based on the quality of the data (randomized controlled trials [RCTs], non-RCTS, meta-analyses, systematic review of the literature, or clinical experience), the amount of evidence (extensive, less extensive, little, or anecdotal clinical experience), and reproducibility of the evidence (highly consistent, single trial, or variable). (A) The categories of evidence and consensus. (B) The categories of preference. A.Categories of evidence and consensus Recommendations are based on level of clinical evidence available and degree of consensus Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate; Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate; Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate; Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate. B.Categories of preference Preferred intervention: Interventions that are based on superior efficacy, safety, and evidence, and, when appropriate, affordability. Other recommended intervention: Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes. Useful in certain circumstances: Other interventions that may be used for selected populations (defined with recommendation). The NCCN Guidelines® for Central Nervous System Cancers Version 1.2023 continues to incorporate and clarify treatment recommendations in relation to the World Health Organization (WHO) 2021 neuropathology updates.2 Information about chemotherapy options previously contained in section BRAIN-D (formerly titled Principles of Brain and Spinal Cord Tumor Systemic Therapy) has been reorganized and now follows directly after the treatment algorithms for the specific tumor type. NCCN Categories of Preference (Table 1) and references have been updated throughout. GLIO-1 has been renamed for better specificity as Adult Glioma: Circumscribed Glioma, which includes pilocytic astrocytoma, subependymal giant cell astrocytoma, ganglioglioma, and pleomorphic xanthoastrocytoma WHO grade 2. GLIO-3 IDH-mutant astrocytoma: To be consistent with the WHO 2021 updated classification of gliomas, high-grade IDH-mutant astrocytomas have been separated into their own treatment guidelines. The recommendations for managing Grade 3 IDH-mutant astrocytomas follow the results of the CATNON study: radiation therapy followed by 12 months of adjuvant temozolomide.3 For Grade 4 treatments, reasonable options include those listed for Grade 3, among others. GLIO-7 glioblastoma: Indeterminate methylguanine methyltransferase (MGMT) status has been moved to the branch for MGMT promoter methylated glioblastoma, as the committee favored the use of temozolomide in this circumstance. GLIO-9 H3-mutated high-grade glioma: A separate algorithm was added for this molecular category. These tumors often behave more aggressively than glioblastoma and tend to be less sensitive to temozolomide; however, due to a lack of other effective therapies for H3-mutated high-grade gliomas, the current treatment recommendations are the same as options for glioblastoma. Adult low-grade glioma: Added the recommendation to consider radiotherapy (RT) dose escalation to 59.4–60 Gy for IDH wild-type diffuse low-grade glioma or CDKN2A/B deleted, IDH-mutated low-grade glioma. These should be treated as high-grade glioma, as these patients have a more aggressive course of disease.4 Re-irradiation of gliomas: The recommendations have been modified to address target volume delineation, suggested RT dose, consideration of different focal RT techniques, and the role of image-guided radiotherapy for recurrent low-grade gliomas. Meningiomas: For WHO grade 2 meningiomas, a new emphasis is placed on using higher RT doses (59.4–60 Gy) for patients with subtotally resected disease or recurrent tumors. Brain metastases: Additional recommendations for when to consider a fractionated SRS approach have been included. The role of preoperative SRS was addressed: Consider preoperative SRS in select cases when logistically feasible to potentially reduce the risk of post-treatment meningeal recurrence (Category 2B). For postoperative SRS, a multifraction approach is preferred for larger surgical cavities, with specific dose and fractionation recommendations provided. More details regarding whole-brain radiation were added, such as cognitive sparing techniques, indications, and dose and fractionation recommendations. The Medical Management section about corticosteroid use now contains a specific recommendation for twice or once-daily dosing of dexamethasone.5 This section underwent extensive updating and reorganization in keeping with recommendations from the 5th edition of WHO Classification of Tumors of the Central Nervous System.2 The panel continues to support and encourage molecular testing of glioblastoma given the potential therapeutic impact of driver mutation discovery. The Molecular Characterization section provides a high-yield list of molecular alterations deemed essential for the correct diagnosis of all gliomas. The list includes mutations of IDH1 R132 and IDH2 R172, TERT promoter, ATRX, EGFR, BRAF V600E, and H3-3A mutation (K27 or G34). The copy number alterations required include 1p19q codeletion, EGFR amplification, gain of chromosome 7, loss of chromosome 10, and CDKN2A/B deletion.2 While this list is not comprehensive, it covers the majority of primary gliomas seen in the community. In cases where histopathology and molecular characterization are equivocal, referral to centers that have advanced molecular diagnostic expertise, including genomic DNA methylation profiling, is strongly recommended. The 2023 NCCN Clinical Practice Guidelines for Central Nervous System Cancers continue to predicate its recommendations on the best data available. The glioma algorithms have been substantially reorganized based on recently revised molecular-based diagnostic classifications and are in need of more subtype-specific clinical trials to foster new recommendations. These revised guidelines are intended to be more user friendly, with the inclusion of the Categories of Preference for chemotherapy choices. BRAIN-C Principles of Radiation for Brain and Spinal Cord Tumors now provides more specific details relative to clinical context and radiation dose and fraction number. The committee has also made progress in incorporating and clarifying the importance of molecular testing in the diagnosis and treatment of primary brain cancers. The text is the sole product of the author and no third party had input or gave support for its writing. Burt Nabors, Department of Neurology, Division of Neuro-oncology; Departments of Neurology and Neurosurgery, O’Neal Comprehensive Cancer Center, Heersink School of Medicine, University of Alabama at Birmingham, Birmingham, Alabama. Jana Portnow, Department of Medical Oncology and Research Therapeutics, City of Hope Comprehensive Cancer Center, Duarte, California. Jona Hattangadi-Gluth, Moores Cancer Center, University of California San Diego, San Diego, California. Craig Horbinski, Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, Illinois. None declared. 1. NCCN. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Central Nervous System Cancers V.1.2023. Philadelphia, PA: National Comprehensive Cancer Network, Inc. 2023. All rights reserved. 2023 [To view the most recent and complete version of the guideline, go online toNCCN.org. [Google Scholar] 2. Louis DN, Perry A, Wesseling P, et al. The 2021 WHO classification of tumors of the central nervous system: a summary. Neuro Oncol. 2021;23(8):1231–1251. [DOI] [PMC free article] [PubMed] [Google Scholar] 3. van den Bent MJ, Tesileanu CMS, Wick W, et al. Adjuvant and concurrent temozolomide for 1p/19q non-co-deleted anaplastic glioma (CATNON; EORTC study 26053-22054): second interim analysis of a randomised, open-label, phase 3 study. Lancet Oncol. 2021;22(6):813–823. [DOI] [PMC free article] [PubMed] [Google Scholar] 4. Appay R, Dehais C, Maurage CA, et al. ; POLA Network. CDKN2A homozygous deletion is a strong adverse prognosis factor in diffuse malignant IDH-mutant gliomas. Neuro Oncol. 2019;21(12):1519–1528. [DOI] [PMC free article] [PubMed] [Google Scholar] 5. Lim-Fat MJ, Bi WL, Lo J, et al. Letter: when less is more: dexamethasone dosing for brain tumors. Neurosurgery. 2019;85(3):E607–E608. [DOI] [PMC free article] [PubMed] [Google Scholar] Articles from Neuro-Oncology are provided here courtesy of Society for Neuro-Oncology and Oxford University Press The National Comprehensive Cancer Network (NCCN) has released Version 3.2025 of the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for ovarian cancer, along with corresponding updates to the NCCN Drugs & Biologics Compendium. These updates include a modification to maintenance therapy recommendations that oncology pharmacists should be aware of when optimizing treatment plans for patients with epithelial ovarian, fallopian tube, or primary peritoneal cancers.Key Change to Maintenance TherapyThe NCCN Guidelines for ovarian cancer has updated maintenance therapy options in section OV-5 of the guidelines. For patients with BRCA1/2 wild-type or unknown status who did not receive bevacizumab (Avastin; Genentech) during primary therapy and are identified as homologous recombination (HR) deficient, the recommended maintenance therapy has been modified to include niraparib (Zejula; GlaxoSmithKline) monotherapy.This adjustment underscores the growing emphasis on tailoring maintenance therapy based on molecular characteristics beyond BRCA mutation status alone. Pharmacists should carefully review patients’ HR deficiency (HRD) testing results to guide treatment selection and ensure appropriate monitoring for PARP inhibitor-associated toxicities, including hematologic adverse effects.Implications for Oncology PharmacistsOncology pharmacists are essential in ensuring the successful implementation of updated treatment strategies, such as the use of niraparib in HR-deficient ovarian cancer. Their expertise in interpreting genetic and HRD testing results, educating patients and providers, managing oral maintenance therapies, and collaborating with multidisciplinary teams enables personalized, evidence-based care that aligns with evolving clinical guidelines.REFERENCENCCN. Clinical Practice Guidelines in Oncology. Ovarian cancer, version 3.2025. July 16, 2025. Accessed July 18, 2025. Colon Cancer, Version 1.2017, NCCN Clinical Practice Guidelines in Oncology. Benson AB 3rd, Venook AP, Cederquist L, Chan E, Chen YJ, Cooper HS, Deming D, Engstrom PF, Enzinger PC, Fichera A, Grem JL, Grothey A, Hochster HS, Hoffe S, Hunt S, Kamel A, Kirilcuk N, Krishnamurthi S, Messersmith WA, Mulcahy MF, Murphy JD, Nurkin S, Saltz L, Sharma S, Shibata D, Skibber JM, Sofocleous CT, Stoffel EM, Stotsky-Himelfarb E, Willett CG, Wu CS, Gregory KM, Freedman-Cass D. Benson AB 3rd, et al. J Natl Compr Canc Netw. 2017 Mar;15(3):370-398. doi: 10.6004/jnccn.2017.0036. J Natl Compr Canc Netw. 2017. PMID: 28275037 The National Comprehensive Cancer Network (NCCN) released its first set of Clinical Practice Guidelines in Oncology (NCCN Guidelines®) in 1996, covering eight tumor types. Today, guidelines are available for more than 60 tumor types, subtypes, and related topics. During the NCCN’s 30th Annual Conference, updates to the guidelines were presented for several of those malignancies. We briefly outline here the latest key recommendations. Bladder Cancer “There have been dramatic changes in the way we think about and address the care of patients with bladder cancer.” —Thomas W. Flaig, MD Updates in bladder cancer were presented by Thomas W. Flaig, MD, of the University of Colorado Cancer Center, Aurora, and Philippe E. Spiess, MD, MS, FACS, FRCSC, of the Moffitt Cancer Center and the University of South Florida, Tampa. Thomas W. Flaig, MD Philippe E. Spiess, MD, MS, FACS, FRCSC Dr. Spiess told The ASCO Post: “There have been a host of new treatments that have been developed for bacillus Calmette-Guérin [BCG]-unresponsive [non–muscle-invasive bladder cancer].” The immune cell–activating interleukin-15 superagonist nogapendekin alfa inbakicept-pmln plus BCG was recently added to the NCCN Guidelines as an initial management option in this clinical context for patients with high-risk disease with carcinoma in situ (with or without papillary) tumors. The current version also encompasses revisions to the Principles of Systemic Therapy section. At the conference, Dr. Flaig highlighted the following key updates for muscle-invasive and metastatic disease: Neoadjuvant gemcitabine plus cisplatin with perioperative durvalumab now represents the “preferred” and only recommendation for perioperative/sandwich therapy (bladder cancer only; category 1). This approach introduces a new treatment strategy in this setting, involving immunotherapy before and after surgery (ie, perioperative/sandwich therapy). Sacituzumab govitecan-hziy was an “other recommended” subsequent-line regimen for locally advanced or metastatic disease (stage IV), but it is now considered “useful in certain circumstances” for both second-line therapy (with prior chemotherapy and immunotherapy) and subsequent-line therapy (with prior chemotherapy, immunotherapy, and enfortumab vedotin-ejfv). The U.S. Food and Drug Addministration (FDA) withdrew the approval for sacituzumab govitecan for advanced or metastatic urothelial carcinoma in late 2024. Fam-trastuzumab deruxtecan-nxki (T-DXd; for HER2-positive, immunohistochemistry [IHC] 3+) has been added into a new table for biomarker-directed therapy, regardless of previous therapy, and recommended as a “preferred” second-line and subsequent-line regimen for some patients with locally advanced or metastatic disease (stage IV). Dr. Flaig discussed some of the organizational changes to the NCCN Guidelines over the past year, specifically related to systemic therapy for locally advanced or metastatic disease (stage IV): “If you looked at these Guidelines a few years ago, we organized [the first-line recommendations] by cisplatin-eligible and -ineligible....” Now, although no longer following this structure, they still offer guidance for the treatment of cisplatin-ineligible patients. “[Regarding second-line therapy, the Guidelines have now] been organized into thinking about previous exposure to immunotherapy and enfortumab vedotin,” he added. There has been a broad incorporation of immune checkpoint inhibitor therapy into the treatment of urothelial carcinoma, with these agents now included in all of the preferred and other recommended first-line systemic therapy regimens for locally advanced or metastatic disease. Differentiated Thyroid Cancer “Thyroid cancers are poster children for precision oncology.” —Lori J. Wirth, MD Lori J. Wirth, MD “Every patient [with differentiated thyroid cancer] who is going to get systemic therapy should have next-generation sequencing testing done,” commented Lori J. Wirth, MD, of Mass General Cancer Center and Harvard Medical School, Boston. In a discussion with The ASCO Post, she highlighted that the “most important” recent updates to the NCCN Guidelines pertain to NTRK and RET gene fusion–specific therapies for those with progressive and/or symptomatic radioactive iodine–refractory papillary carcinoma, radioactive iodine–refractory follicular carcinoma, and oncocytic carcinoma: Repotrectinib was added as “useful in certain circumstances” for the treatment of NTRK gene fusion–positive advanced solid tumors. The recommendation for selpercatinib for RET gene fusion–positive tumors (useful in certain circumstances) has been revised to reflect its expanded FDA approval for use in pediatric patients aged at least 2 years. “Coming soon is an international phase III trial of second-line dabrafenib plus trametinib in BRAF V600E–positive [papillary] thyroid cancer,” Dr. Wirth told The ASCO Post, which may impact future recommendations in the NCCN Guidelines. Of note, the combination is currently listed as “useful in certain circumstances” in this setting (in the absence of satisfactory alternatives) for the abovementioned populations of patients with progressive and/or symptomatic disease. Although not FDA-approved, pembrolizumab plus lenvatinib (for disease progression on lenvatinib) and pemetrexed plus carboplatin (for disease progression after prior treatment) are also listed as “useful in certain circumstances” for these patients in the NCCN Guidelines, based on supportive data from recent studies. Other recent updates regarding differentiated thyroid cancer include the following: Encompassing the abovementioned and other revisions, the section for systemic therapy has been modified. The algorithms for the diagnosis as well as the primary treatment of papillary and oncocytic carcinoma have been modified. Modifications were made to the algorithms for the management of follicular and papillary carcinomas after total thyroidectomy with radioactive iodine, as well as to the algorithms for the treatment of locally recurrent, advanced, and/or metastatic radioactive iodine–refractory disease. Resectable Gastroesophageal Adenocarcinoma and Peritoneal-Limited Disease “It is a very exciting time for developing new treatments in gastric cancer.” —Harry H. Yoon, MD, MHS Based largely on recently published data from the ESOPEC trial, perioperative chemotherapy with FLOT (fluorouracil plus leucovorin, oxaliplatin, and docetaxel) became the new “preferred” primary treatment for medically fit patients with resectable locally advanced esophageal and esophagogastric junction adenocarcinomas, replacing the previous standard of preoperative chemoradiation therapy. This represents the “biggest change this year in the [NCCN Guidelines for Esophageal and Esophagogastric Junction Cancers] for this indication,” according to Harry H. Yoon, MD, MHS, of the Mayo Clinic Comprehensive Cancer Center, Rochester, Minnesota.   Harry H. Yoon, MD, MHS Travis E. Grotz, MD, MS Although preoperative chemoradiation therapy is no longer “preferred” and has been downgraded to category 2A (from category 1), deciding when to use this previous standard is “complicated” and requires multidisciplinary discussion, according to Dr. Yoon. A footnote was thus added, providing criteria that essentially support preoperative chemoradiation therapy for those who likely would have been excluded from the ESOPEC trial. An algorithm for the treatment of peritoneal-limited disease was introduced in the first version of the 2024 NCCN Guidelines for Gastric Cancer, recommending cytoreductive surgery with gastrectomy and intraperitoneal chemotherapy/hyperthermic intraperitoneal chemotherapy (HIPEC)/pressurized intraperitoneal aerosol chemotherapy as an additional treatment in patients with a low peritoneal cancer index (defined as ≤ 10) and stable or improved disease after at least 6 months of systemic therapy and a multidisciplinary discussion. In a subsequent version, the recommendation was updated to require a minimum of 3 months of systemic therapy, swap the order of the surgical procedures, and remove pressurized intraperitoneal aerosol chemotherapy; data supporting the use of this drug delivery system are limited, so it is now recommended only in the context of a clinical trial. “[The abovementioned recommended additional treatment regimen] should only be done at institutions with considerable experience with gastrectomy, cytoreduction, and HIPEC,” commented Travis E. Grotz, MD, MS, also of the Mayo Clinic Comprehensive Cancer Center, after presenting the updates. Advanced Gastroenteropancreatic Neuroendocrine Tumors “In terms of therapies, we have a number of new tools in the toolkit.” —Emily Bergsland, MD Emily Bergsland, MD Emily Bergsland, MD, of the University of California, San Francisco (UCSF) Helen Diller Family Comprehensive Cancer Center, discussed the consequential updates to the NCCN Guidelines for well-differentiated advanced gastroenteropancreatic neuroendocrine tumors resulting from influential clinical trials. Cabozantinib, which is now FDA-approved based on the CABINET trial, was recently added to the NCCN Guidelines for the following clinical scenarios: Treatment of well-differentiated locoregionally advanced and/or distant metastatic grade 1 or 2 neuroendocrine tumors of the gastrointestinal tract (preferred; category 1 if previously treated with everolimus or lutetium Lu-177 dotatate); Treatment of well-differentiated locoregionally advanced and/or distant metastatic grade 1 or 2 pancreatic neuroendocrine tumors (preferred; category 1 if previously treated with everolimus, lutetium Lu-177 dotatate, or sunitinib); Treatment of well-differentiated locally advanced or metastatic (unresectable with clinically significant tumor burden or evidence of disease progression) grade 3 neuroendocrine tumors with favorable biology. Findings from the NETTER-1 trial supported the initial FDA approval of peptide receptor radionuclide therapy with lutetium Lu-177 dotatate for progressive gastroenteropancreatic neuroendocrine tumors after somatostatin analog therapy. Building on this, NETTER-2 evaluated its use as a first-line treatment in patients with higher-risk tumors, leading to its inclusion in the NCCN Guidelines in the following clinical scenarios: First-line treatment of well-differentiated locoregionally advanced and/or distant metastatic grade 1 or 2 somatostatin receptor (SSTR)-positive neuroendocrine tumors of the gastrointestinal tract and pancreas (if the Ki67 index is ≥ 10% and there is a clinically significant tumor burden; preferred); Treatment of well-differentiated locally advanced or metastatic grade 3 SSTR-positive neuroendocrine tumors with favorable biology (eg, Ki67 index < 55%) (if unresectable with a clinically significant tumor burden or evidence of disease progression) (category 2B). “There have been changes to pathological classification over the past 8 years or so, with well-differentiated grade 3 neuroendocrine tumors added for tumors arising in the pancreas in 2017 and the gastrointestinal tract in 2019, which then led to a new section of the Guidelines [and subsequent revisions to it (abovementioned)] to address management of this new group of tumors,” Dr. Bergsland told The ASCO Post. “This is an evolving area, as new studies are starting to emerge that specifically include this group.” Metastatic Colorectal Cancer “[In this era, we have] a range of treatment options that have changed the face of [advanced and metastatic colorectal cancer].” —Alan P. Venook, MD Alan P. Venook, MD Alan P. Venook, MD, of the UCSF Helen Diller Family Comprehensive Cancer Center, highlighted two recent “game-changing” updates to the systemic therapy landscape for metastatic colorectal cancer that are now reflected in the NCCN Guidelines. Both are supported by clinical trial data presented during the 2025 ASCO Gastrointestinal Cancers Symposium. CheckMate 8HW: The recommendation for nivolumab plus ipilimumab in microsatellite instability–high (MSI-H)/mismatch repair–deficient (dMMR) disease has expanded to include first-line treatment (category 2A), with category 2B status in cases where intensive therapy is not advised because of toxicity concerns. BREAKWATER: Encorafenib plus cetuximab and FOLFOX (leucovorin, fluorouracil, and oxaliplatin) is now recommended as an initial intensive therapy (category 2A) and as a second-line and subsequent biomarker-directed therapy (category 2B) for patients with advanced or metastatic BRAF V600E–mutated microsatellite stable (MSS)/mismatch repair–proficient (pMMR) (or MSI-H/dMMR or POLE/POLD1 mutation–positive with an ultra-hypermutated phenotype that is ineligible for or progressed on checkpoint inhibitor immunotherapy) disease. Of note, although panitumumab was not evaluated in the trial, it is listed as an alternative to cetuximab. Other recent updates to the systemic therapy landscape include the following additions: Nivolumab plus ipilimumab for colorectal cancer (MSI-H/dMMR or POLE/POLD1-mutated with an ultra-hypermutated phenotype; if checkpoint inhibitor monotherapy was previously received); Additional checkpoint immunotherapy options (ie, cemiplimab-rwlc, retifanlimab-dlwr, toripalimab-tpzi, tislelizumab-jsgr) for patients with MSI-H/dMMR or POLE/POLD1 mutations with an ultra-hypermutated phenotype in the following clinical scenarios: —Neoadjuvant treatment for rectal cancer with resectable synchronous liver only and/or lung only metastases; —Initial treatment of immunotherapy-naive rectal cancer with resectable metachronous metastases; —Any line of treatment for immunotherapy-eligible, immunotherapy-naive colorectal cancer, with the option for continuation following disease status reassessment; FOLFIRINOX (leucovorin, fluorouracil, irinotecan, and oxaliplatin) as a neoadjuvant chemotherapy option for MSS/pMMR rectal cancer with resectable synchronous liver only and/or lung only metastases. A recent update in surgical and locoregional management emerged from the COLLISION trial of colorectal cancer liver metastases. Per the NCCN Guidelines, thermal ablation is equivalent to resection for the treatment of select small-sized lesions (≤ 3 cm). Dihydropyrimidine dehydrogenase (DPYD) catabolizes fluoropyrimidines, and genetic variants that alter its enzymatic activity may increase the risk of toxicity for patients treated with these drugs. This pharmacogenetic phenomenon is recognized by the NCCN Guidelines for colorectal cancer, which now recommend discussing DPYD genetic variant testing prior to fluoropyrimidine therapy and considering it in the context of the patient’s individual circumstances. Small Cell Lung Cancer “The pace of progress was quite slow initially with small cell lung cancer.... [But] in 2024, we have had two exciting developments....” —Saiama N. Waqar, MD, MSCI Saiama N. Waqar, MD, MSCI The key updates to the NCCN Guidelines for Small Cell Lung Cancer were centered on the further integration of immunotherapy into the treatment paradigm, according to Saiama N. Waqar, MD, MSCI, of Washington University School of Medicine, St. Louis. Supported by the DeLLphi-301 trial, tarlatamab-dlle was added as a subsequent therapy option for patients with a chemotherapy-free interval of more than (other recommended) and up to (preferred) 6 months. Consolidation therapy with durvalumab was added as a “preferred” regimen for patients with limited-stage disease who did not experience disease progression after systemic therapy plus concurrent radiation therapy, informed by the ADRIATIC trial, with a subsequent change in its NCCN Category of Recommendation (category 1 from 2A) designation. Nonmetastatic NSCLC “I urge everybody to discuss these cases in your multidisciplinary tumor board...[and to] get good molecular testing....” —Jonathan W. Riess, MD, MS Patients with tumors of at least 4 cm or node-positive non–small cell lung cancer (NSCLC) who do not have actionable oncogene driver mutations such as EGFR mutations and ALK fusions should be evaluated for preoperative therapy, with a strong consideration for the combination of immune checkpoint inhibitors plus chemotherapy, per the updated NCCN Guidelines. Jonathan W. Riess, MD, MS, of the University of California (UC) Davis Comprehensive Cancer Center, Sacramento, discussed two trials of immunotherapy before and after surgery, combined with preoperative chemotherapy, that informed some of the most recent additions to the Guidelines: AEGEAN (durvalumab; category 1) and CheckMate 77T (nivolumab; category 1). Of note, based on the ALINA trial, adjuvant alectinib is now recommended for ALK-positive disease (category 1). Jonathan W. Riess, MD, MS Based on the LAURA trial, osimertinib is now listed as a consolidation therapy option for patients with unresectable stage II or III NSCLC, an Eastern Cooperative Oncology Group performance status score of 0 or 1, and no disease progression after definitive concurrent chemoradiation therapy; category 1 for stage III, category 2A for stage II. Relapsed or Refractory Hodgkin Lymphoma “The benefits of checkpoint inhibitors do appear to persist beyond [disease] progression.” —Ryan C. Lynch, MD Primary treatment with nivolumab plus AVD (doxorubicin, vinblastine, and dacarbazine) was recently promoted to “preferred” (from “other recommended”) status and category 1 (from 2A) for stage III to IV classical Hodgkin lymphoma, and it was added in combination with involved-site radiation therapy for stage I or II unfavorable disease in the NCCN Guideline. Ryan C. Lynch, MD, of Fred Hutchinson Cancer Center and the University of Washington School of Medicine, Seattle, emphasized the importance of exploring the next steps when front-line immunotherapies fail. Ryan C. Lynch, MD The recommendations for systemic therapy for relapsed or refractory disease have been updated in the latest version of the Guidelines, with PD-1 inhibitors serving as the current “backbone” of management. Essentially, the revised approach emphasizes that, “if a checkpoint inhibitor hasn’t been given upfront, it should be part of the second-line regimen,” according to Dr. Lynch. In a discussion with The ASCO Post, he outlined the key modifications to the treatment algorithms regarding immune checkpoint inhibitor–based second-line therapy: For high-dose therapy/autologous stem cell rescue–eligible patients with primary refractory disease or relapse within 3 months, such therapy is now “preferred” in the absence of prior exposure to immune checkpoint inhibitors. High-dose therapy/autologous stem cell rescue–ineligible patients who underwent immune checkpoint inhibitor therapy and experienced disease progression at least 3 (vs 6) months after their last exposure are now eligible. This year also brought three key modifications to NCCN’s recommendations for patients who are refractory to at least three prior lines of subsequent therapy, Dr. Lynch told The ASCO Post. Despite concerns over durability, two pembrolizumab-containing doublet regimens (with vorinostat or decitabine) were added, given the limited options in this setting. Involved-site radiation therapy is now also recommended. Multiple Myeloma “We have made dramatic progress in the management of multiple myeloma.” —Shaji K. Kumar, MD Shaji K. Kumar, MD, of the Mayo Clinic Comprehensive Cancer Center, Rochester, Minnesota, and Natalie S. Callander, MD, of the University of Wisconsin and William S. Middleton Memorial Veterans’ Hospital, Madison, presented recent data in multiple myeloma, which have contributed in part to changes in the recommendations within the NCCN Guidelines over the past year. Shaji K. Kumar, MD Natalie S. Callander, MD Recent changes indicate a shift toward quadruplet therapies in the management of transplant candidates. The combination of daratumumab, lenalidomide, bortezomib, and dexamethasone (category 1) has been promoted from an “other recommended” to “preferred” primary therapy for these patients, whereas two triplets (bortezomib, lenalidomide, and dexamethasone [category 1] and carfilzomib, lenalidomide, and dexamethasone) are now classified as “other recommended.” Another recent addition to the list of “other recommended” regimens is isatuximab-irfc, bortezomib, lenalidomide, and dexamethasone. Updates to the maintenance therapy recommendations for this population include the following: Lenalidomide with carfilzomib or daratumumab are now classified as “other recommended” regimens. Still considered “useful in certain circumstances,” the recommendation for bortezomib plus lenalidomide was modified to bortezomib with or without lenalidomide. Similarly, quadruplet regimens are emerging as primary therapies for nontransplant candidates. The regimen of isatuximab, bortezomib, lenalidomide, and dexamethasone was recently added as a “preferred” option for nonfrail patients younger than age 80 (category 1). Here are other updates in primary therapy for the transplant-ineligible population: The regimens of daratumumab, bortezomib, melphalan, and prednisone (category 1) and daratumumab, cyclophosphamide, bortezomib, and dexamethasone have been removed as “other recommended” regimens; the latter is now classified as “useful in certain circumstances.” The regimen isatuximab, carfilzomib, lenalidomide, and dexamethasone was added as “useful in certain circumstances” (category 2B). A new column was recently added to the table of “preferred” regimens for previously treated patients (one to three prior lines), which includes the following recommendations for those whose disease is refractory to anti-CD38 agents: Carfilzomib, lenalidomide, and dexamethasone (category 1); Carfilzomib, pomalidomide, and dexamethasone; Pomalidomide, bortezomib, and dexamethasone (category 1); Elotuzumab, pomalidomide, and dexamethasone (after two prior therapies, including lenalidomide and a proteasome inhibitor); Ixazomib, pomalidomide, and dexamethasone (after two prior therapies, including an immunomodulatory drug and a proteasome inhibitor, and with disease progression on/within 60 days of completion of the last therapy). The bortezomib-refractory column now includes elotuzumab, pomalidomide, and dexamethasone, recommended after two prior therapies, including lenalidomide and a proteasome inhibitor. In the lenalidomide-refractory column, the abovementioned regimen was moved under a heading to reflect this indication, and the regimen of selinexor, bortezomib, and dexamethasone (category 1) was removed and reclassified to “other recommended.” Further updates to the list of “other recommended” options after one to three prior lines of therapy include the addition of daratumumab, carfilzomib, pomalidomide, and dexamethasone. Another option in this category—pomalidomide, cyclophosphamide, and dexamethasone—was recently promoted to category 1 (from 2A; after two prior therapies, including an immunomodulatory drug and a proteasome inhibitor, and disease progression on or within 60 days of completion of the last therapy). Anti–B-cell maturation antigen and anti–G protein–coupled receptor, class C group 5 member D bispecific antibodies are now key treatment options for heavily pretreated patients, according to the presenters. Thus, talquetamab-tgvs and teclistamab-cqyv are now listed in the NCCN Guidelines as “useful in certain circumstances” for those who underwent at least three prior lines of therapy. DISCLOSURE: Dr. Flaig has received consulting fees from Criterium; has received grant or research support from Agensys, Astellas Pharma US, AstraZeneca, Bristol Myers Squibb, Genentech, Janssen Pharmaceutica Products, Merck & Co., sanofi-aventis U.S., and SeaGen; has disclosed intellectual property rights and equity interest or stock options with Aurora Oncology; and has served as a scientific advisor for Criterium and Janssen Pharmaceutica Products. Dr. Spiess has served as a consultant to MyCareAlgorithm in developing educational resources for patients and health-care providers. Dr. Wirth has received consulting fees from AbbVie, Bayer HealthCare, Bicara Therapeutics, Coherus BioSciences, Eisai, Eli Lilly and Company, EMD Serono, Exelixis, Illumina, Merck & Co., Nested Therapeutics, PDS Biotechnology, Replimune Group, and Tubulis GmbH; and has served as a scientific advisor for Eisai, Eli Lilly and Company, and Ellipses Pharma. Dr. Yoon has received grant or research support from Amgen, BeiGene, Bristol Myers Squibb, and Merck & Co.; has received honoraria from Amgen, Astellas Pharma US, BeiGene, Elevation Oncology, and Merck & Co.; and has served as a scientific advisor for Amgen, Astellas Pharma US, BeiGene, Elevation Oncology, and Merck & Co. Dr. Grotz has received consulting fees from Agenus and Ferranova. Dr. Bergsland has received grant or research support from Boehringer Ingelheim GmbH, Merck & Co., and RAYZbio. Dr. Venook has served as a scientific advisor for Amgen, Bristol Myers Squibb, Exact Sciences Corporation, Exelixis, GSK, Intera Oncology, and Pfizer. Dr. Waqar has received consulting fees from AstraZeneca, Boehringer Ingelheim GmbH, Daiichi Sankyo, Gilead Sciences, Janssen Pharmaceuticals, Amgen, and Pfizer; and has received institutional grant or research support from AbbVie, Advenchen Laboratories, AstraZeneca, Elevation Oncology, Nuvalent, Genentech, Gilead Sciences, Janssen Pharmaceuticals, Regeneron Pharmaceuticals, Ribon Therapeutics, and Takeda Pharmaceuticals North America. Dr. Riess has received consulting fees from Daiichi Sankyo and OncoHost; has received grant or research support from ArriVent BioPharma, AstraZeneca, Boehringer Ingelheim GmbH, IO Biotech, Merck & Co., Novartis, Nuvalent, Prelude Therapeutics, Revolution Medicines, SeaGen, and Summit Therapeutics; and has received honoraria from Amgen, Bristol Myers Squibb, Catalyst Pharmaceuticals, Genentech, GSK, Janssen Pharmaceutica Products, Merck & Co., Merus N.V., Pfizer, and Regeneron Pharmaceuticals. Dr. Lynch has received consulting fees from AbbVie, ADC Therapeutics SA, and Janssen Pharmaceutica Products; has received grant or research support from Allogene Therapeutics, Cyteir Therapeutics, Genentech, Incyte, Janssen Pharmaceutica Products, Pfizer, and RAPT Therapeutics; and has received honoraria from Merck & Co. Dr. Kumar has received consulting fees from Moderna; has received grant or research support from AbbVie, Amgen, Bristol Myers Squibb, CARsgen Therapeutics, GSK, Janssen Pharmaceutica Products, Oricell Therapeutics, Regeneron Pharmaceuticals, Roche Laboratories, sanofi-aventis U.S., and Takeda Pharmaceuticals North America; and has served as a scientific advisor for AbbVie, Amgen, Bristol Myers Squibb, GSK, Janssen Pharmaceutica Products, Regeneron Pharmaceuticals, Roche Laboratories, sanofi-aventis U.S., and Takeda Pharmaceuticals North America. Dr. Callander reported no conflicts of interest. Receiving a pancreatic cancer diagnosis can be overwhelming, but trusted information can make a meaningful difference. That’s why we’re proud to once again support the NCCN Guidelines for Patients: Pancreatic Cancer, a vital resource created by experts and available for free to patients and caregivers. These guidelines empower individuals to be active participants and feel more prepared for every step in their care journey. “The NCCN Guidelines for Patients: Pancreatic Cancer is a trusted, expert-developed resource that offers the latest information on treatment options, medical terminology, questions to ask your doctor, and much more – all in clear, compassionate language,” says Amy Reiss, Director of Patient Programs at the Hirshberg Foundation. “We proudly support this updated version, ensuring that patients and families have access to the knowledge they need right from the start. As Director of Patient Programs, I believe it is one of the most valuable tools we can provide at diagnosis.” The 2025 edition includes important updates that reflect the latest advancements in pancreatic cancer care, including: The use of PET/MRI imaging for cancer staging. Expanded molecular testing recommendations to include ALK, NRG1, ROS1, and FGFR2 gene fusions. Addition of HER2 overexpression testing to help guide targeted therapy decisions. New guidance for managing anorexia to support patients’ nutritional health. Updated pain management protocols to improve patient comfort and outcomes. Additional treatment options recommended based on performance status, such as NALIRIFOX, erdafitinib, zenocutuzumab-zbco, repotrectinib, and fam-trastuzumab deruxtecan-nxki. Thanks to our ongoing partnership with the NCCN Foundation, these materials are available online and free to access. This resource reflects our commitment to education, empowerment, and compassionate support for everyone facing pancreatic cancer. “We are so thankful for the support from our patient advocacy collaborator, the Hirshberg Foundation for Pancreatic Cancer Research!” says Mary Ellen Martelli, Project Coordinator at the NCCN Foundation. “NCCN Foundation appreciates this relationship, which empowers those with a pancreatic cancer diagnosis to get the information and support needed to make informed decisions about their cancer journey.” We invite you to explore the latest guidelines and share them with anyone in need. By working together, we’re helping people feel more prepared and less alone. Access the NCCN Guidelines for Patients: Pancreatic Cancer

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