

NCCN Flash Updates™

4th Quarter 2015

The following report contains NCCN Flash Updates™ relative to the fourth quarter of 2015, listed in chronological order with the most recent updates first.

December 22, 2015

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Non-Small Cell Lung Cancer. These NCCN Guidelines® are currently available as Version 3.2016.

- Systemic Therapy for Metastatic Disease; ALK Positive (NSCL-18)
 - Subsequent therapy
 - Alectinib added as a treatment option as a category 2A recommendation for the following indications:
 - Asymptomatic progression
 - Symptomatic progression and brain metastases
 - Symptomatic progression and multiple systemic metastases
 - Progression on subsequent (second-line and beyond) therapy
 - Ceritinib added as a treatment option as a category 2A recommendation for the following indication:
 - Symptomatic progression and brain metastases
 - First-line systemic therapy options; squamous cell carcinoma; PS 0-2 (NSCL-F 3 of 4)
 - The combination regimen of cisplatin/gemcitabine/necitumumab added as a category 3 recommendation for PS 0-2.
- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

**For your reference, the previous update (Version 2.2016) to the NCCN Guidelines for Non-Small Cell Lung Cancer, published on November 23, 2015, is available at the following link:*
http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf

December 21, 2015

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Occult Primary. These NCCN Guidelines® are currently available as Version 1.2016.

- The Immunohistochemistry Markers section of the guidelines has been modified extensively. (OCC-A)
- Two chemotherapy regimens, Irinotecan/Carboplatin and Irinotecan/Gemcitabine, are new to Adenocarcinoma. (OCC-B 2 of 4)
- Principles of Radiation Therapy is new to the guidelines. (OCC-C)

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NCCN has published updates to the NCCN Guidelines and NCCN Compendium® for Hepatobiliary Cancers. These NCCN Guidelines are currently available as Version 1.2016.

- Hepatocellular Carcinoma
 - For liver imaging studies, a footnote was amended regarding PET/CT: "At least a 3-phase liver protocol CT or MRI including late arterial phase and portal venous phase to determine perfusion characteristics, extent and number of lesions, vascular anatomy, and extrahepatic disease. PET/CT is not adequate for diagnosis or as the only evaluation of liver disease; it could be considered for metastatic disease. Bruix J and Sherman M. Management of Hepatocellular Carcinoma: an Update. Hepatology 2011;53(3):1020-1022. doi: 10.1002/hep.24199" (For HCC-1, HCC-2, and HCC-3)
 - Under "Surgical Assessment" for "UNOS criteria" a footnote was added: "Some patients beyond the Milan criteria can be considered for transplantation. Extended criteria/downstaging protocols are available at selected centers and through UNOS." (HCC-5)
 - Under "Surveillance" for patients with cancer that is potentially resectable or transplantable, operable by performance status or comorbidity: "Refer to a hepatologist for a discussion of antiviral therapy for carriers of hepatitis," was added to the pathway. (HCC-5)
 - Principles of Surgery (HCC-B):
 - For circumstances where hepatic resection is potentially curative, a statement was amended: "Adequate liver function (generally Child-Pugh Class A without portal hypertension, but small series show feasibility of limited resections in patients with mild portal hypertension)," and a reference was added: "Santambrogio R, Kluger MD, Costa M, et al. Hepatic resection for hepatocellular carcinoma in patients with Child-Pugh's A cirrhosis: Is clinical evidence of portal hypertension a contraindication? HPB (Oxford). 2013 Jan;15 (1):78-84."
 - Principles of Locoregional Therapy (HCC-C 1 of 3)
 - Under "Ablation", a statement regarding sorafenib as adjuvant therapy was revised: "Sorafenib may be appropriate following ablative therapy in patients with adequate liver function once bilirubin returns to baseline if there is evidence of residual/recurrent tumor not amenable to additional local therapies. The safety and efficacy of adjuvant sorafenib following ablation is being investigated in an ongoing clinical trial," was removed and replaced with: "Sorafenib should not be used as adjuvant therapy post-ablation." A corresponding reference was removed: "Printz C. Clinical trials of note. Sorafenib as adjuvant treatment in the prevention of disease recurrence in patients with hepatocellular carcinoma (HCC) (STORM). Cancer 2009;115:46. (<http://clinicaltrials.gov/show/NCT00692770>)" and replaced with: "Bruix J, Takayama T, Mazzaferro V, et al. Adjuvant sorafenib for hepatocellular carcinoma after resection or ablation (STORM): a phase 3, randomised, double-blind, placebo-controlled trial. Lancet Oncol 2015;16(13):1344-54."
- Gallbladder Cancer
 - Under "Workup": "Consider CEA" and "Consider CA 19-9", a footnote was added: "CEA and CA 19-9 are baseline tests and should not be done to confirm diagnosis." (For GALL-3, GALL-4, INTRA-1, and EXTRA-1)
 - For the surveillance of patients post-resection (GALL-5)
 - The following statement was amended: "Consider imaging every 6 mo for 2 y if clinically indicated, then annually up to 5 y" and "Consider CEA and CA 19-9 as clinically indicated"
 - A footnote was amended: "There are no data to support aggressive surveillance. There should be a patient/physician discussion regarding appropriate follow-up schedules/imaging."

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- Intrahepatic Cholangiocarcinoma (INTRA-1)
 - The presentation statement was amended: "Isolated intrahepatic mass (imaging characteristics consistent with malignancy but not consistent with hepatocellular carcinoma) (See NCCN Guidelines for Occult Primary Cancers)"
 - Under "Workup" when intrahepatic cholangiocarcinoma is suspected: "*Consider AFP*" was added.
- Extrahepatic Cholangiocarcinoma (EXTRA-1)
 - Under "Workup" when extrahepatic cholangiocarcinoma is suspected, the following statement was amended: "Consider endoscopic ultrasound (EUS) *after surgical consultation.*"

December 9, 2015

NCCN has published *NEW* NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) with NCCN Evidence Blocks™ for the following disease type:

- Kidney Cancer, Version 2.2016

NCCN has published updates to the NCCN Drugs & Biologics Compendium (NCCN Compendium®) to reflect updates to the 2016 Version of the corresponding NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®):

- Non-Hodgkin's Lymphomas, V 1.2016

December 4, 2015

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bone Cancer. These NCCN Guidelines® are currently available as Version 2.2016.

- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

**For your reference, the previous update (Version 1.2016) to the NCCN Guidelines for Bone Cancer, published on October 16, 2015, is available at the following link: http://www.nccn.org/professionals/physician_gls/pdf/bone.pdf*

NCCN has published updates to the NCCN Guidelines for Cancer-Related Fatigue. These NCCN Guidelines are currently available as Version 1.2016.

- The 7th bullet under Assessment of Treatable Contributing Factors has been modified to include "drug interactions." It links to the NCCN Guidelines for Older Adult Oncology. (FT-4)
- Yoga is a new bullet under Interventions for Patients on Active Treatment and Post-Treatment, Nonpharmacologic. It has been designated category 1. (FT-5 and FT-6)
- Bright white light therapy has been added as an intervention for Active Treatment, Nonpharmacologic. The following footnote corresponds: "Bright white light therapy of 10,000 lux is most frequently self-administered in

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the early morning for 30-90 minutes. Timing needs to be adjusted for those who sleep during the day." (FT-5)

- Footnote "m" has been modified to include "Optimal dosing and schedule have not been established for use of psychostimulants in older adults and patients with cancer." (FT-5)
- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

December 2, 2015

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Melanoma. These NCCN Guidelines® are currently available as Version 2.2016.

- Adjuvant Treatment for Stage III Disease (ME-4)
 - "High-dose ipilimumab (category 2B)" added as an option for Stage III (sentinel positive) and Stage III (clinically positive node[s]).
 - Footnote s is new: "Adjuvant ipilimumab is associated with improvement in recurrence-free survival. Its impact on overall survival has not been reported. The recommended dose of ipilimumab (10 mg/kg) was associated with adverse events which led to the discontinuation of treatment in 52% of patients. There was a 1% drug-related mortality rate."
 - Footnote t is new: "The clinical trial excluded patients with sentinel lymph node metastases ≤1 mm in size and who did not undergo CLND. The decision to use ipilimumab should be based on risk of recurrence balanced against the risk of treatment-related toxicity. It is unclear whether the decision should be based on CLND."
- Primary Treatment for Stage III in-transit Disease (ME-5)
 - "Intralesional injection with talimogene laherparepvec (T-VEC) (category 1)" added as an option with corresponding footnote z, "T-VEC was associated with a response rate (lasting ≥6 months) of 16% in highly selected patients with unresectable metastatic melanoma. Efficacy was most pronounced in Stage IIIB, IIIC and Stage IV-M1a disease and in patients who were treatment naive."
- Treatment of Recurrence
 - Local, Satellite, and/or In-transit recurrence: "Intralesional injection with T-VEC (category 1)" added as an option with corresponding footnote z. (ME-8)
 - Nodal recurrence with unresectable or systemic disease (ME-9):
 - "Systemic therapy" is now listed as a "preferred" option.
 - "Intralesional injection with T-VEC" added as an option with corresponding footnote z.
 - Adjuvant Treatment for patients who have had a complete lymph node dissection and/or a complete resection of the nodal recurrence: "High-dose ipilimumab (category 2B)" added as a treatment option with corresponding footnotes.
- Treatment of Metastatic Disease (ME-10)
 - Patients with disseminated (unresectable) distant metastatic disease:
 - "Systemic therapy" is now listed as a "preferred" option.

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- "Intralesional injection with T-VEC" added as an option with corresponding footnote ii, "T-VEC has shown a response rate (lasting ≥6 months) of 16% in highly selected patients with Stage IV-M1a disease (skin, subcutaneous, and/or remote nodes)."
- Systemic Therapy For Metastatic or Unresectable Disease (ME-E 1 of 5)
 - For both first-line and second-line or subsequent targeted therapy, the recommended combination regimens are listed as "preferred" over single-agent therapy options.
 - First-line Therapy: "Vemurafenib/cobimetinib (category 1)" added as a preferred treatment option with corresponding footnote 4, "In previously untreated patients with unresectable Stage IIIC or Stage IV disease, the combination of vemurafenib/cobimetinib was associated with improved PFS and response rate when compared to vemurafenib alone. The impact on overall survival compared to single agent vemurafenib is unknown."
 - Second-line or Subsequent Therapy: "Vemurafenib/cobimetinib" added as a preferred treatment option.

**For your reference, the previous update (Version 1.2016) to the NCCN Guidelines for Melanoma, published on October 23, 2015, is available at the following link:*

http://www.nccn.org/professionals/physician_gls/pdf/melanoma.pdf

November 25, 2015

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Colon Cancer. These NCCN Guidelines® are currently available as Version 2.2016.

- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

**For your reference, the previous update (Version 1.2016) to the NCCN Guidelines for Colon Cancer, published on November 4, 2015, is available at the following link: http://www.nccn.org/professionals/physician_gls/pdf/colon.pdf*

NCCN has published updates to the NCCN Guidelines and NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Cervical Cancer. These NCCN Guidelines are currently available as Version 1.2016.

- Primary Treatment (Fertility Sparing) (CERV-2)
 - New footnote "g" defining negative margins added: "Negative for invasive disease or histologic high-grade squamous intraepithelial lesion (HSIL) at margins."
- Primary Treatment (Non-fertility Sparing) (CERV-4)
 - New footnote "p" regarding adjuvant hysterectomy for Stage IB2 and Stage IIA2 added: "This approach can be considered in patients whose extent of disease or uterine anatomy precludes adequate coverage by brachytherapy."
- Surveillance (CERV-10)

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- Fifth bullet regarding patient education revised to include smoking cessation and a link to the NCCN Guidelines for Smoking Cessation.
- Principles of Radiation Therapy (CERV-B)
 - External Beam Radiation Therapy
 - Fourth bullet revised: "...Very careful attention to detail and reproducibility (including consideration of target and normal tissue definitions, patient and internal organ motion, soft tissue deformation, and rigorous dosimetric and physics quality assurance) is required for proper delivery of IMRT and related highly conformal technologies. *Routine image guidance, such as cone-beam CT (CBCT), may be helpful in defining daily internal soft tissue positioning.*"
 - New bullet added: "*Concepts regarding the gross target volume (GTV), clinical target volume (CTV), planning target volume (PTV), organs at risk (OARs) and dose-volume histogram (DVH) have been defined for use in conformal radiotherapy, especially for IMRT.*"
 - Brachytherapy
 - New bullet added: "*Point A, representing a paracervical reference point, has been the most widely used, validated, and reproducible dosing parameter used to date. However, limitations of the Point A dosing system include the fact that it does not take into account the three-dimension shape of tumors, nor individual tumor to normal tissue structure correlations. There are increasing efforts to use and standardize image-based volumetric brachytherapy approaches using MRI, CT or ultrasound - international validation efforts are underway.*"
- Chemotherapy Regimens for Recurrent or Metastatic Cervical Cancer (CERV-D)
 - First-line combination therapy:
 - "Carboplatin/paclitaxel" changed to "Carboplatin/paclitaxel (category 1 for patients who have received prior cisplatin therapy)."
 - "Carboplatin/paclitaxel/bevacizumab" added as an option.
 - Second-line therapy: "Albumin-bound paclitaxel (category 2B)" added as an option.
- The Discussion section has been updated to reflect the changes in the algorithm (MS-1).

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Kidney Cancer. These NCCN Guidelines® are currently available as Version 2.2016.

- Relapsed/Stage IV and surgically unresectable disease with predominant clear cell histology (KID-3)
 - For subsequent therapy after a tyrosine kinase inhibitor, the following options were added:
 - Cabozantinib (category 1)
 - Nivolumab (category 1)
 - A corresponding footnote was added to cabozantinib and nivolumab: "Based on the results of phase III trials, eligible patients should preferentially receive this agent over everolimus. See Discussion."
- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

**For your reference, the previous update (Version 1.2016) to the NCCN Guidelines for Kidney Cancer, published*

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on September 14, 2015, is available at the following link:

http://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf

NCCN has published updates to the NCCN Guidelines for Non-Hodgkin's Lymphomas. These NCCN Guidelines are currently available as Version 1.2016

- Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)
 - First-line therapy
 - Cladribine was removed as a recommendation for CLL without del (11q) or del (17p)/TP53 mutation for patients ≥70 years and younger patients with significant comorbidities.
 - Relapsed/refractory therapy
 - Idelalisib + rituximab was changed from a category 2A to a category 1 recommendation for all patients.
 - Idelalisib monotherapy is included with a category 2A recommendation for all patients.
 - Bendamustine ± rituximab was moved as the first option under chemoimmunotherapy for CLL without del (11q) or del (17p)/TP53 mutation and for CLL with del (11q) for patients ≥70 years and younger patients with significant comorbidities.
- Follicular Lymphoma
 - Second-line Consolidation or Extended Dosing (FOLL-B 1 of 3)
 - Obinutuzumab maintenance for rituximab refractory disease (category 2B) (1 g every 8 wks for total of 12 doses) was added.
- Mantle Cell Lymphoma (MCL)
 - Stage II bulky, III, IV (MANT-3)
 - Algorithms were extensively revised to include separate treatment options for aggressive and indolent MCL.
 - The following definition was added for indolent MCL: "(SOX11- [IGHV mutated], leukemic non-nodal CLL-like with splenomegaly, low tumor burden, Ki-67 proliferation fraction <30%)."
 - Observation is recommended for patients with indolent MCL.
 - First-line Therapy (MANT-A)
 - Less aggressive therapy: Cladribine + rituximab was changed from a category 2A to a category 2B recommendation.
 - First-line consolidation (MANT-A)
 - Candidate for HDT/ASCR, "± rituximab maintenance" was added to high-dose therapy with autologous stem cell rescue.
 - Not a candidate for HDT/ASCR, "rituximab maintenance" (category 1 following RCHOP)" was added as an option.
- Diffuse Large B-Cell Lymphoma (DLBCL)
 - For primary mediastinal large B-cell lymphoma, the first-line therapy options were organized in "order of preference." (BCEL-B 1 of 3)
 - A new page with a definition and suggested treatment recommendations for double hit lymphoma was added. (BCEL-B 3 of 3)
 - First-line Therapy (BCEL-C)
 - Patients with Poor Left Ventricular Function or Very Frail patients

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- RGCVP (rituximab, gemcitabine, cyclophosphamide, vincristine, and prednisolone) was added.
 - RCNOP (rituximab, cyclophosphamide, mitoxantrone, vincristine, and prednisone) was removed.
- Patients >80 Years of Age with Comorbidities
 - RGCVP (rituximab, gemcitabine, cyclophosphamide, vincristine, and prednisolone) was added.
- Peripheral T-Cell Lymphomas (PTCL)
 - Second-line and Subsequent therapy (TCEL-B)
 - Recommendations were reorganized by preferred and alternate/regimens and into 3 groups: PTCL-NOS and EATL, AITL, and ALCL.
 - Intention to proceed to transplant
 - Belinostat was changed from a category 2B to category 2A recommendation for all subtypes.
 - Dose-adjusted EPOCH was removed as a recommendation for all subtypes.
 - For alternative regimens, gemcitabine and lenalidomide and GVD (gemcitabine, vinorelbine, and liposomal doxorubicin) were added to appropriate subtypes.
 - No intention to transplant
 - For alternative single agents, lenalidomide was added to appropriate subtypes.
- Mycosis Fungoides/Sézary Syndrome
 - Bortezomib was added as a category 3 recommendation to Systemic Therapies, Category B (second-line therapies) and Systemic Therapies, Category C (MFSS-A)
- Primary Cutaneous CD30+ T-Cell Lymphoproliferative Disorders
 - Interferon alpha was removed as a primary treatment option for primary cutaneous ALCL (multifocal lesions). (PCTLD-4)
- Extranodal NK/T-Cell Lymphoma, nasal type
 - Treatment options for Stage I and II (nasal) were combined.
 - Induction therapy options (previously based on risk factors) are now based on performance status (unfit for chemotherapy and fit for chemotherapy). (NKTL-2)
 - Sandwich chemoradiation was added as an option for induction therapy in selected patients fit for chemotherapy. (NKTL-2)
 - Combination chemotherapy regimen (NKTL-B 1 of 2)
 - SMILE regimen (4–6 cycles) is recommended only for advanced stage disease.
 - GELOX (gemcitabine, pegaspargase, oxaliplatin) was added as an option.
 - Sequential chemoradiation (NKTL-B 1 of 2)
 - SMILE regimen followed by RT 45–50.4 Gy x 2–4 cycles is recommended only for stage I-II disease.
 - VIPD followed by RT 45–50.4 Gy was removed.
 - Sandwich chemoradiation: GELOX (2 cycles) followed by RT 56 Gy followed by GELOX (2–4 cycles) was added as an option. (NKTL-B 1 of 2)
- Post-Transplant Lymphoproliferative Disorders (PTLD)
 - T-cell PTLD was added as a new subtype with the following recommendations: (PTLD-1)
 - Other than reduction of immunosuppression (RI), there are no established treatments.
 - Treatment with multiagent T-cell regimens may be considered; however, autotransplant may not be appropriate.
 - Suggested treatment regimens (PTLD-A)

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- A bullet was added, "For CD20 negative monomorphic T-cell post-transplant lymphomas, the regimens recommended for B-cell post-transplant lymphomas are used without rituximab."
- RCHOEP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone, etoposide) was removed as an option for concurrent chemoimmunotherapy.
- Castleman's Disease
 - Lenalidomide + rituximab was added as an option for relapsed/refractory disease. (CD-4)
- Special Considerations for the Use of Small-Molecule Inhibitors (Ibrutinib and Idelalisib) (NHODG-E)
 - The use of ibrutinib before and after a surgical procedure was clarified as follows: "Ibrutinib should be held 3 days before and after a minor surgical procedure and 7 days before and after a major surgical procedure. Ibrutinib should not be given concomitantly with warfarin."
 - The following recommendations were added for the management of atrial fibrillation associated with ibrutinib administration:
 - Consider non-warfarin anticoagulation
 - Monitor carefully
 - Consider switching to alternate therapy
 - Patients with recurrent atrial fibrillation that is not medically controllable should be changed to idelalisib.
 - The following recommendations were added for the management of hypertension associated with ibrutinib:
 - Hypertension associated with ibrutinib should be managed with anti-hypertensives as appropriate.
 - Ibrutinib should only be discontinued for uncontrollable hypertension.

November 24, 2015

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Non-Small Cell Lung Cancer. These NCCN Guidelines® are currently available as Version 2.2016.

- Systemic Therapy for Metastatic Disease; Sensitizing EGFR Mutation Positive (NSCL-17)
 - Subsequent therapy
 - Osimertinib added as a treatment option as a category 2A recommendation for the following indications:
 - Asymptomatic progression
 - Symptomatic progression and isolated systemic metastasis
 - Symptomatic progression and multiple systemic metastases
 - Progression on subsequent therapy
- Footnote "pp" added: Osimertinib is approved for patients with metastatic EGFR T790M mutation-positive tumors, as determined by an FDA-approved test or other validated laboratory developed test performed in a CLIA-approved laboratory.
- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

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**For your reference, the previous update (Version 2.2016) to the NCCN Guidelines for Non-Small Cell Lung Cancer, published on October 27, 2015, is available at the following link:
http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf*

NCCN has published updates to the NCCN Guidelines and NCCN Compendium® for Breast Cancer. These NCCN Guidelines are currently available as Version 1.2016.

- Non-Invasive Breast Cancer
 - Ductal Carcinoma In Situ
 - Modified the first sentence in footnote “h”: “Complete axillary lymph node dissection should not be performed in the absence of evidence of invasive cancer or proven axillary metastatic disease in women with apparent pure DCIS” by adding “or mammographically detected DCIS with microcalcifications.” (DCIS-1)
 - Included aromatase inhibitor as an endocrine therapy option for postmenopausal women (DCIS-2)
- Invasive Breast Cancer
 - Added a link to the NCCN Guidelines for Older Adult Oncology for special treatment considerations to pages BINV-1,-2,-3,-5,-6,-7,-8, and -9)
 - Locoregional Treatment of Clinical Stage I, IIA, or IIB disease or T3, N1, M0 (BINV-2)
 - Lumpectomy with surgical axillary staging, ≥4 positive axillary nodes:
 - Made the recommendation radiation therapy for “infraclavicular region, supraclavicular area, internal mammary nodes, and any part of the axillary bed at risk”, a category 1
 - Lumpectomy with surgical axillary staging 1-3 positive axillary nodes:
 - Changed the recommendation for “Strongly consider radiation therapy to infraclavicular, supraclavicular area, internal mammary nodes, and any part of the axillary bed at risk” from category 2B to category 2A.
 - Locoregional Treatment of Clinical Stage I, IIA, or IIB disease or T3, N1, M0 (BINV-3)
 - Total mastectomy with surgical axillary staging, ≥4 positive axillary nodes:
 - Made the recommendation radiation therapy for “infraclavicular region, supraclavicular area, internal mammary nodes, and any part of the axillary bed at risk” a category 1.
 - Total mastectomy with surgical axillary staging, 1-3 positive axillary nodes:
 - Changed the recommendation for “Strongly consider radiation therapy to infraclavicular, supraclavicular area, internal mammary nodes, and any part of the axillary bed at risk” from category 2B to category 2A.
- Systemic Adjuvant Treatment – Hormone Receptor-Positive - HER2-Negative Disease (BINV-6)
 - Added a footnote to Consider 21-gene RT-PCR assay indicating “Other prognostic multigene assays may be considered to help assess risk of recurrence but have not been validated to predict response to chemotherapy.”
- Preoperative Systemic Therapy (BINV-12 and BINV-15)
 - “Endocrine therapy alone may be considered for receptor-positive disease in postmenopausal patients.” has been clarified as “Endocrine therapy alone with an aromatase inhibitor (preferred option for postmenopausal women; given along with ovarian suppression for premenopausal women) or tamoxifen may be considered for patients with hormone-receptor positive disease.”
 - Added a link to Principles of Preoperative Systemic Therapy, a new section in the Guidelines.
- Surveillance/Follow-Up (BINV-16)
 - Added the following new recommendations:
 - “Periodic screening for changes in family history and referral to genetic counseling as necessary.”
 - “Routine imaging of reconstructed breast is not indicated.”

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- "In the absence of clinical signs and symptoms suggestive of recurrent disease, there is no indication for laboratory or imaging studies for metastases screening."
 - Added a new footnote for "Mammography every 12 mo" stating "Studies indicate that annual mammograms are the appropriate frequency for surveillance of breast cancer patients who have had breast-conserving surgery and radiation therapy with no clear advantage to shorter interval imaging. Patients should wait 6 to 12 months after the completion of radiation therapy to begin their annual mammogram surveillance. Suspicious findings on physical examination or surveillance imaging might warrant a shorter interval between mammograms."
 - Added healthy diet and limited alcohol intake to the following bullet "Evidence suggests that active lifestyle, healthy diet, limited alcohol intake and achieving and maintaining an ideal body weight (20–25 BMI) may lead to optimal breast cancer outcomes."
- Treatment of Recurrence (BINV-18)
 - Added a new footnote, "Multidisciplinary approach is especially important in the management of breast cancer recurrence to consider all potential treatment options for optimal outcomes."
 - Systemic Treatment of Recurrent or Stage IV Disease (BINV-22)
 - Added Ado-trastuzumab emtansine (T-DM1) to first line therapy.
 - Changed "trastuzumab ± chemotherapy" to "trastuzumab + chemotherapy"
- Fertility and Birth Control (BINV-C)
 - Modified the first bullet: "All premenopausal patients should be informed about the potential impact of chemotherapy on fertility and asked about their desire for potential future pregnancies. Patients who may desire future pregnancies should be referred to fertility specialists before chemotherapy and/or endocrine therapy to discuss the options based on patient specifics, disease stage, and biology (which determine the urgency and type and sequence of treatment). Timing and duration allowed for fertility preservation, options inclusive of oocyte and embryo cryopreservation as well as evolving technologies, and the probability of successful pregnancies subsequent to completion of breast cancer therapy are also to be discussed."
- Principles of Reconstruction Following Surgery (BINV-H)
 - First paragraph, added the following "However, breast reconstruction should not interfere with the appropriate surgical management of the cancer or the scope of appropriate surgical treatment for this disease. Coordinating consultation and surgical treatment with a reconstructive surgeon should be executed within a reasonable time frame."
- Principles of Radiation Therapy (BINV-I)
 - This section has been updated and reformatted.
- Adjuvant Endocrine Therapy (BINV-J)
 - Premenopausal at diagnosis:
 - Changed tamoxifen for 5 y + ovarian suppression or ablation from a category 2B to a category 1 recommendation.
 - Added aromatase inhibitor for 5y + ovarian suppression or ablation (category 1) as an option.
 - Included a new footnote "Aromatase inhibitor or tamoxifen for 5 y plus ovarian suppression should be considered, based on SOFT and TEXT clinical trial outcomes, for premenopausal women at higher risk of recurrence (i.e. young age, high grade tumor, lymph node involvement, Pagani, NEJM 2014, Prudence, NEJM 2014). Survival data still pending."
- Preoperative/Adjuvant Therapy Regimens (BINV-K)
 - Removed the following regimens from the list of regimens for preoperative/adjuvant chemotherapy:
 - FAC/CAF (fluorouracil/doxorubicin/cyclophosphamide)

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- FEC/CEF (cyclophosphamide/ epirubicin/fluorouracil)
- Principles of Preoperative Systemic Therapy (BINV-L)
 - This section is a new addition to the Guidelines.
- Endocrine Therapy for Recurrent or Stage IV Disease (BINV-N)
 - Added Palbociclib + fulvestrant (category 1) as a therapeutic option with the following footnote:
 - For postmenopausal women with hormone-receptor positive, HER2-negative metastatic breast cancer that has progressed on endocrine therapy or premenopausal women receiving ovarian suppression with an LHRH agonist.
- Chemotherapy Regimens for Recurrent or Metastatic Breast Cancer (BINV-O)
 - Other agents for HER2-positive disease:
 - Ado-trastuzumab emtansine (T-DM1) added a treatment option.
 - Trastuzumab alone was removed as a treatment option.
 - Agents for trastuzumab-exposed HER2-positive disease:
 - For "Trastuzumab + other agents" a new footnote was added stating "Trastuzumab may be safely combined with all non-anthracycline containing preferred and other single agents listed above for recurrent or metastatic breast cancer."
- Phyllodes (PHYLL-1)
 - Revised footnote "a": "FNA or core biopsy may not distinguish a fibroadenoma from a phyllodes tumor in some cases. The sensitivity of core biopsy for the diagnosis of phyllodes tumor is greater than that of FNA biopsy, but neither core biopsy nor FNA biopsy can always differentiate phyllodes tumors from fibroadenomas. In cases with clinical suspicion for phyllodes tumor, excision of the lesion may be needed for definitive pathologic classification."

November 20, 2015

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Uterine Neoplasms. These NCCN Guidelines® are currently available as Version 2.2016.

- The Discussion section has been updated to reflect the changes in the endometrial carcinoma and uterine sarcoma algorithms. (MS-1)
- Uterine Sarcoma
 - Systemic Therapy: Trabectedin added as a single-agent option with corresponding footnote "3" that states, "For uLMS that has been treated with a prior anthracycline-containing regimen." (UTSARC-A)

**For your reference, the previous update (Version 1.2016) to the NCCN Guidelines for Uterine Neoplasms, published on October 15, 2015, is available at the following link:*
http://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf

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November 19, 2015

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Palliative Care. These NCCN Guidelines® are currently available as Version 1.2016.

- For non-specific nausea and vomiting, olanzapine is new to the page. (PAL-15)
- “Consider glycopyrrolate 0.2-0.4 mg IV q 4 hr prn” is a new bullet under antidiarrheal interventions. (PAL-19)
- Administer octreotide has been modified to include: “if prognosis >8 weeks, consider long lasting release (LAR) or depot injection.” (PAL-21)
- “Encourage the patient and family to limit CPR with the use of DNR/DNAR/AND” is new to the page. (PAL-30)
- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

NCCN has published updates to the NCCN Guidelines for Distress Management. These NCCN Guidelines are currently available as Version 3.2015.

- Global Changes
 - The Psychological/Psychiatric Treatment algorithms were revised extensively, including:
 - The pathways were revised to include criteria to be consistent with the Diagnostic and Statistical Manual of Mental Disorders (5th ed.)
 - New pathways were added for “Bipolar and Related Disorders,” “Trauma- and Stressor-Related Disorders,” and “Obsessive Compulsive and Related Disorders.”
 - The titles for the following Psychological/Psychiatric Treatment algorithms were revised:
 - “Dementia” and “Delirium” were clarified as “*Neurocognitive Disorders*”
 - “Mood Disorders” changed to “*Depressive Disorders*”
 - “Schizophrenia/Psychotic Disorders” changed to “*Schizophrenia Spectrum and Other Psychotic Disorders*”
 - “Adjustment Disorder” changed to “*Trauma-and Stressor-Related Disorders: Adjustment Disorders*”
 - “Substance-Related Disorder/Abuse” changed to “*Substance-Related and Addictive Disorders*”

**For your reference, the previous update (Version 2.2015) to the NCCN Guidelines for Distress Management, published on July 31, 2015, is available at the following link:*
http://www.nccn.org/professionals/physician_gls/pdf/distress.pdf

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November 13, 2015

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Cancer- and Chemotherapy-Induced Anemia. These NCCN Guidelines® are currently available as Version 2.2016.

- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

**For your reference, the previous updates (Version 1.2016) to the NCCN Guidelines for Cancer- and Chemotherapy-Induced Anemia, published on July 31, 2015, are available at the following link:*

http://www.nccn.org/professionals/physician_gls/pdf/anemia.pdf

November 12, 2015

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Smoking Cessation. These NCCN Guidelines® are currently available as Version 2.2015.

- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

**For your reference, the previous updates (Version 1.2015) to the NCCN Guidelines for Smoking Cessation, published on March 9, 2015, are available at the following link:*

http://www.nccn.org/professionals/physician_gls/pdf/smoking.pdf

NCCN has published updates to the NCCN Guidelines and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Prostate Cancer. These NCCN Guidelines are currently available as Version 1.2016.

- Initial Prostate Cancer Diagnosis (PROS-1)
 - Footnote “b” modified to: “Men with clinically localized disease may consider the use of tumor-based molecular assays. Retrospective case cohort studies have shown that molecular assays performed on biopsy or prostatectomy specimens provide prognostic information independent of NCCN risk groups. These include, but are not limited to, likelihood of death with conservative management, likelihood of biochemical progression after radical prostatectomy or external beam therapy, and likelihood of developing metastasis after radical prostatectomy or salvage radiotherapy. See Discussion section.”
- Intermediate Risk Group (PROS-4)
 - Added a new footnote for patients with favorable intermediate-risk prostate cancer, “Patients with favorable intermediate-risk prostate cancer (predominant Gleason grade 3 [i.e., Gleason score 3 + 4 = 7], and percentage of positive biopsy cores < 50 percent, and no more than one NCCN intermediate risk factor) can be considered for active surveillance. See Discussion section.”
 - Modified an existing footnote “Active surveillance of *unfavorable* intermediate and high-risk clinically localized cancers is not recommended in patients with a life expectancy >10 years (category 1).”

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- High- and Very High-Risk Groups (PROS-5)
 - “EBRT + ADT (2-3 y) + docetaxel” was added as an initial therapy option for high- and very high-risk groups with the following footnote: “Addition of 6 cycles of docetaxel every 3 weeks without prednisone administered following the completion of radiation.”
- Radical Prostatectomy Biochemical Failure (PROS-7), Radiation Therapy Recurrence (PROS-8), and Systemic Therapy For Progressive Castration-Naive Disease (PROS-9)
 - Footnote “t” modified to: “Observation involves monitoring the course of disease with the expectation to begin ADT when symptoms develop or PSA changes to suggest symptoms are imminent. See Principles of Active Surveillance and Observation (PROS-C).”
- Radiation Therapy Recurrence (PROS-8)
 - Following candidate for local therapy:
 - Changed the recommendation for TRUS biopsy to “Consider TRUS biopsy.”
 - If TRUS biopsy positive, studies negative for distant metastases: added pelvic lymph node dissection (PLND) to radical prostatectomy (RP) recommendation.
- Systemic Therapy For Progressive Castration-Naive Disease (PROS-9)
 - Separated treatment options for M0 and M1 disease.
 - Added a new footnote stating, “Intermittent ADT can be considered for men with M0 or M1 disease to reduce toxicity. See Principles of Androgen Deprivation Therapy (PROS-F).”
 - M1 disease, modified the treatment option to read: “Continuous ADT and docetaxel 75 mg/m² with or without prednisone for 6 cycles.”
 - Modified footnote “u” by adding “Patients with low volume disease have less certain benefit from early treatment with docetaxel combined with ADT.”
 - Following small cell, changed treatment option “docetaxel-based regimen” to “docetaxel/carboplatin.”
- Systemic Therapy for M0 CRPC (PROS-10), Systemic Therapy for M1 CRPC (PROS-11), and Subsequent Systemic Therapy for M1 CRPC (PROS-12 and PROS-13)
 - Ketoconazole, added “± hydrocortisone.” This change was made throughout the guideline where ketoconazole is recommended.
 - DES or other estrogen, added the following footnote: “DES has cardiovascular and thromboembolic side effects at any dose but frequency is dose and agent dependent. DES should be initiated at 1 mg/day and increased, if necessary, to achieve castrate levels of serum testosterone (<50 ng/dL). Other estrogens delivered topically or parenterally may have less frequent side effects but data are limited.” This change was made throughout the guideline where DES or other estrogen is recommended.
- Principles of Imaging (PROS-B)
 - Modified the following bullet “Newer technology using 18F-NaF as the tracer for a PET scan *or hybrid imaging bones scans* can be used as a diagnostic staging study. These tests appear to have greater sensitivity than bone scan. However, there is controversy about how the results of 18F-NaF PET bone scan should be acted upon since all phase 3 clinical trials to date have used progression criteria on bone scans.
 - Modified the following bullet: “MRI may be considered in patients after RP when PSA fails to fall to undetectable levels or when an undetectable PSA becomes detectable and increases on 2 or more subsequent determinations, or after RT for rising PSA or positive DRE if the patient is a candidate for additional local therapy. *MRI-US fusion biopsy may improve the detection of higher grade (Gleason score >7) cancers.*”
- Principles of Active Surveillance and Observation (PROS-C, 2 of 2)
 - Added the following bullet under Advantages of active surveillance:

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- About 2/3 of men eligible for active surveillance will avoid treatment.
- Added the following bullets under Disadvantages of active surveillance
 - About 1/3 of men will require treatment, although treatment delays do not seem to impact cure rate.
 - Periodic follow-up prostate biopsies may be necessary.
- Removed the following bullets under Disadvantages of active surveillance:
 - Risk of progression and/or metastases
 - Subsequent treatment may be more complex with increased side effects
 - Nerve sparing may be more difficult, which may reduce chance of potency preservation after surgery
 - Increased anxiety
 - Requires frequent medical exams and periodic biopsies, which are not without complications
 - Uncertain long-term natural history of prostate cancer
- Principles of Radiation Therapy (PROS-D)
 - Primary external beam radiation therapy: modified the statement “Patients with high-risk *and very high-risk* cancers *should receive* neoadjuvant/concomitant/adjuvant ADT for a total of 2 to 3 y *if comorbidities allow* (category 1). *Pelvic lymph node irradiation can be considered.*”
 - Primary brachytherapy: modified the statement “Patients with a very large prostate or very small prostate, symptoms of bladder outlet obstruction (high IPSS), or a previous transurethral resection of the prostate are more difficult to implant and may suffer increased risk of side effects. Neoadjuvant ADT may be used to shrink the prostate to an acceptable size; however, increased toxicity would be expected from ADT and prostate size may not decline *in some men despite neoadjuvant ADT. Potential toxicity of ADT must be balanced against the potential benefit of target reduction.*”
- Principles of Immunotherapy and Chemotherapy (PROS-G)
 - Added 2 new bullets:
 - “Men who have not demonstrated definitive evidence of progression on prior docetaxel therapy, may be retreated with docetaxel.”
 - “No chemotherapy regimen to date has demonstrated improved survival or quality of life after cabazitaxel, and participation in clinical trials should be encouraged.”

November 9, 2015

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Testicular Cancer. These NCCN Guidelines® are currently available as Version 1.2016.

- Nonseminoma, Post-chemotherapy management (TEST-11)
 - For a complete response with negative markers and an original stage of Stage IIA, S1; Stage IIB, S1; Stage IIC; or Stage IIIA, the treatment option of “Bilateral RPLND ± nerve-sparing in selected cases (category 2B)” was modified as “Bilateral RPLND + nerve-sparing in selected cases (category 2B).”
- Nonseminoma, Second-line therapy (TEST-12)
 - For Favorable prognosis, “Clinical trial (preferred)” was added.

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- Follow-up
 - Seminoma, for Table 1, 2 and 3 “Abdominal/Pelvic CT” was changed to “Abdominal ± Pelvic CT.” (TEST-A)
 - Nonseminoma, for Table 5, 6, 7 and 8, “Abdominal/Pelvic CT” was changed to “Abdominal ± Pelvic CT.” (TEST-B)
- The Discussion section was updated to reflect the changes in the algorithm. (MS-1)

NCCN has published updates to the NCCN Guidelines and the NCCN Compendium® for Colon Cancer, Rectal Cancer, and Anal Carcinoma. These NCCN Guidelines are currently available as Version 1.2016.

- NCCN Guidelines for Colon Cancer
 - Primary Treatment of Colon Cancer (COL-2)
 - The category of “Clinical T4b” added with the recommendation of “Consider neoadjuvant chemotherapy” followed by “Colectomy with en bloc removal of regional lymph nodes followed by surgery.”
 - Locally unresectable or medically inoperable: Treatment recommendations modified to include the option of RT with “Chemotherapy for Advanced Disease.” Subsequent treatment options added with the option of “Surgery ± IORT or Chemotherapy.”
 - Pathologic Stage and Adjuvant Therapy (COL-3)
 - Pathologic stage T3, N0, M0 (MSI HIGH) added with the recommendation of no adjuvant therapy.
 - Surveillance (COL-3 and COL-4)
 - Surveillance, bullet 3 modified: Chest/abdominal/pelvic CT *every 6-12 mo (category 2B for frequency < 12 mo) annually* for up to 5 y for patients at high risk for recurrence.
 - Workup of Suspected or Proven Metastatic Synchronous Adenocarcinoma (COL-5)
 - The following bullet added: Determination of tumor MSI status.
 - Workup of Metachronous Metastases (COL-9)
 - Footnote “II” modified: Determination of tumor gene status for RAS (KRAS exon 2 and non-exon 2, and NRAS) and BRAF. *Determination of tumor MSI status. See Principles of Pathologic Review (COL-A 4 of 5) - KRAS, NRAS and BRAF Mutation Testing and Microsatellite Instability (MSI) or Mismatch Repair Deficiency (dMMR) Testing.*
- NCCN Guidelines for Rectal Cancer
 - Primary Treatment of Rectal Cancer (REC-3)
 - T1,NX with high-risk features or T2,Nx
 - The treatment option of neoadjuvant chemo/RT was added followed by transabdominal resection.
 - Chemo/RT options: Capecitabine/RT or infusional 5-FU/RT (preferred for both) or bolus 5-FU/leucovorin/RT.
 - Footnote “n” added: Bolus 5-FU/leucovorin/RT is an option for patients not able to tolerate capecitabine or infusional 5-FU. (Also added throughout Guidelines where bolus 5-FU/leucovorin/RT is listed as a recommendation.)

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- Neoadjuvant Therapy for Rectal Cancer (REC-4)
 - Radiation therapy used in chemo/RT clarified as “long-course” RT.
 - The option of short-course RT added with the qualifier that it is not recommended for T4 tumors.
 - Footnote “o” added: Evaluation for short-course RT should be in a multidisciplinary setting, with a discussion of the need for down-staging and the possibility of long-term toxicity.
- Workup of Metastatic Disease (REC-6, REC-7, REC-9)
 - Footnote “v” modified: Determination of tumor gene status for RAS (KRAS exon 2 and non-exon 2, and NRAS) and BRAF. *Determination of tumor MSI status*. See Principles of Pathologic Review (REC-A 5 of 6) - KRAS, NRAS and BRAF Mutation Testing and *Microsatellite Instability (MSI) or Mismatch Repair Deficiency (dMMR) Testing*.
- Surveillance (REC-8)
 - Surveillance recommendation added only for patients after transanal excision.
 - Proctoscopy (with EUS or MRI) every 3-6 mo for the first 2 years, then every 6 mo for a total of 5 years (for patients treated with transanal excision only).
- Principles of Surgery (REC-B 1 of 3)
 - The following bullet removed: Laparoscopic surgery is preferred in the setting of a clinical trial.
 - The following text added: Some studies have shown that laparoscopy is associated with similar short- and long-term outcomes when compared to open surgery, whereas other studies have shown that laparoscopy is associated with higher rates of circumferential margin positivity and incomplete TME. Therefore, minimally invasive resection may be considered based on the following principles:
 - The surgeon should have experience performing minimally invasive proctectomy with total mesorectal excision.
 - It is not indicated for locally advanced disease with a threatened or high risk circumferential margin based on staging. For these high risk tumors, open surgery is preferred.
 - It is not indicated for acute bowel obstruction or perforation from cancer.
 - Thorough abdominal exploration is required.
- NCCN Guidelines for Colon and Rectal Cancers
 - Treatment of Resectable Synchronous Metastases (COL-6) (REC-6) or Metachronous Metastases (COL-10) (REC-10)
 - Local therapy added as a treatment option, in combination or as an alternate to resection. Resection noted as “preferred” over local therapy.
 - Footnote added: Resection is preferred over locally ablative procedures (eg, image-guided ablation or SBRT). However, these local techniques can be considered for liver oligometastases.
 - Treatment of Unresectable Metachronous Metastases (COL-11) (COL-C) (REC-11) (REC-E)
 - Footnote modified where bevacizumab, ziv-aflibercept, and ramucirumab are listed as treatment options: “Bevacizumab is the preferred anti-angiogenic agent based on toxicity and/or cost.”
 - Chemotherapy for Advanced or Metastatic Disease (COL-C) (REC-E)
 - The regimen of trifluridine + tipiracil was added as a subsequent therapy option for patients with disease progression after oxaliplatin- and irinotecan-based chemotherapy.
 - Footnote added: Oxaliplatin may be given either over 2 hours, or may be infused over a shorter time at a rate of 1 mg/m²/minute. Leucovorin infusion should match infusion time of oxaliplatin. Cercet A,

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- Park V, Yaeger RD, et al. Oxaliplatin can be safely infused at a rate of 1mg/m²/min. J Clin Oncol 33, 2015 (suppl; abstr e14665).
- Principles of Pathologic review (COL-A 4 of 5) (REC-A 5 of 6)
 - Microsatellite Instability (MSI) section modified: "...or Mismatch Repair Deficiency (dMMR) Testing"
 - Bullet 1 modified: Lynch Syndrome tumors screening (ie, IHC for dMMR or PCR for MSI) should be ~~considered performed~~ for all patients with colorectal cancer diagnosed at age ≤70 y and also those >70 y who meet the Bethesda guidelines. See NCCN Guidelines for Colorectal Cancer Screening.
 - Bullet 2 added: The presence of a BRAF V600E mutation in the setting of MLH1 absence would preclude the diagnosis of Lynch Syndrome
 - Bullet 3 added: MMR or MSI testing should also be performed for all patients with stage II disease, because stage II MSI-H patients may have a good prognosis and do not benefit from 5-FU adjuvant therapy.
 - Bullet 4 added: MSI testing should also be performed for all patients with metastatic disease.
 - Footnote "*" added: IHC for dMMR and PCR for MSI are different assays measuring the same biological effect.
 - NCCN Guidelines for Anal Carcinoma
 - Workup of Anal Carcinoma (ANAL-1, ANAL-2)
 - Bullet 3 modified: Chest/abdominal/~~pelvic~~ CT or + pelvic CT or MRI
 - Bullet 3, sub-bullet 1 modified: Consider PET scan for T2-4, N0 or Any T, N+
 - Principles of Radiation Therapy (ANAL-B)
 - Bullet 6 modified: For T2 lesions ~~with residual disease after 45 Gy~~, T3/4 lesions, or N1 lesions, an additional boost of 9-14 Gy in 1.8-2 Gy fractions to the original primary tumor volume and involved nodes plus a 2-2.5 cm margin is usually delivered.
 - Bullet 7 modified: The consensus of the panel is that IMRT ~~may be used in place of~~ is preferred over 3-D conformal RT in the treatment of anal carcinoma. IMRT requires expertise and careful target design to avoid reduction in local control by so-called "marginal-miss." The clinical target volumes for anal cancer used in the RTOG-0529 trial have been described in detail. *The outcome results of RTOG-0529 have been reported.* (Kachnic LA, Winter K, Myerson RJ, et al. RTOG 0529: a phase 2 evaluation of dose-painted intensity modulated radiation therapy in combination with 5-fluorouracil and mitomycin-C for the reduction of acute morbidity in carcinoma of the anal canal. Int J Radiat Oncol Biol Phys 2013;86:27-33.)

October 28, 2015

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Basal Cell Skin Cancer, Dermatofibrosarcoma Protuberans, Merkel Cell Carcinoma, and Squamous Cell Skin Cancer. These NCCN Guidelines® are currently available as Version 1.2016.

- Merkel Cell Carcinoma
 - Primary and Adjuvant Treatment: Clinical N0 Disease (MCC-2)
 - For management of the draining nodal basin, footnote "g" was added: "In the head and neck region, risk of false-negative SLNBs is higher due to aberrant lymph node drainage and frequent

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- presence of multiple SLN basins. If SLNB is not performed or is unsuccessful, consider irradiating nodal beds for subclinical disease (See MCC-B)."
- Treatment of Clinical M1 Disease
 - Under "Follow-up", footnote "p" was added: "As immunosuppressed patients are at high risk for recurrence, more frequent follow-up may be indicated. Immunosuppressive treatments should be minimized as clinically feasible." (MCC-5)
- Principles of Radiation Therapy (MCC-B)
 - The MCC-B page was divided into two pages, "*Primary Tumor Site*" and "*Draining Nodal Basin*" and extensively revised.
- Principles of Excision (MCC-C)
 - Under "Surgical Approaches", for the 2nd sub-bullet, "When tissue sparing is of critical importance" was removed and modified to: "Techniques for more exhaustive histologic margin assessment may be considered (Mohs technique, modified Mohs, CCPDMA), *provided they do not interfere with SLNB when indicated.*"
 - Under "Reconstruction"
 - A bullet was removed: "Immediate reconstruction is recommended in most cases."
 - The following bullet was modified: "It is recommended that any reconstruction involving extensive undermining or tissue movement be delayed until negative histologic margins are verified *and SLNB is performed if indicated.*"
- Dermatofibrosarcoma Protuberans
 - Principles of Pathology (DFSP-A)
 - Footnote "2", "FS-DPSF should be noted when present as it is associated with a poor prognosis," was added to the bullet describing fibrosarcomatous transformation. (FS-DFSP)
 - Principles Of Excision (DFSP-B)
 - The following statement was added to the "Goal" section: "Specimens from debulking excisions should be examined to identify fibrosarcomatous transformation (FS-DFSP) if present."
- Basal Cell Skin Cancer
 - Primary Treatment (BCC-2)
 - Under "Curettage and electrodesiccation", the 1st bullet statement, "In non-hair bearing areas," was changed to: "*Excluding terminal hair-bearing areas, such as scalp, pubic, axillary regions, and beard area in men.*"
 - Adjuvant Treatment (BCC-3)
 - "Vismodegib" was replaced with "a hedgehog pathway inhibitor" and footnote "n", "Current FDA approved hedgehog pathway inhibitors include vismodegib and sonidegib," under "Adjuvant Treatment" in the "Standard excision" pathway, when margins are positive: "If residual disease is present, and further surgery and RT are contraindicated, consider multidisciplinary tumor board consultation (consider *a hedgehog pathway inhibitor* or clinical trials)."
 - Under "Adjuvant Treatment", in the "Mohs or resection" pathway, when margins are positive, a treatment option was added: "RT *and/or multidisciplinary tumor board consultation (consider a hedgehog pathway inhibitorⁿ or clinical trial)*"
 - Recurrence (BCC-4)

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- Under "Follow-up", footnote "o" was added: "If no further skin cancers are identified in the first 2 years, then less frequent follow-up may be appropriate."
- Under "Recurrence", "Regional" and "Distant metastases" pathways were combined into a "Nodal or distant metastases" pathway.
- "Vismodegib" was replaced with "a hedgehog pathway inhibitor" and footnote "n", "Current FDA approved hedgehog pathway inhibitors include vismodegib and sonidegib", in the "Nodal or distant metastases" pathway: "Multidisciplinary tumor board consultation (consider a hedgehog pathway inhibitor or clinical trials)."
- Risk Factors for Recurrence (BCC-A)
 - Footnote "3", describing "Aggressive growth pattern", was revised: "Having morpheaform, basosquamous (metatypical), sclerosing, mixed infiltrative, or micronodular features is any portion of the tumor. *In some cases basosquamous (metatypical) tumors may be prognostically similar to SCC. Clinicopathologic consultation is recommended.*"
- Squamous Cell Skin Cancer
 - Primary Treatment (SCC-2)
 - Under "Curettage and electrodesiccation", the 1st bullet statement, "In non-hair bearing areas", was changed to: "*Excluding terminal hair-bearing areas, such as scalp, pubic, axillary regions, and beard area in men.*" Risk Factors for Local Recurrence or Metastases (SCC-A)
 - Under "Pathology", the following risk factors were revised:
 - "Adenoid (acantholytic), adenosquamous (showing mucin production), or desmoplastic or basosquamous (metatypical) subtypes"
 - "Perineural, lymphatic, or vascular involvement"
 - Identification and Management of High-Risk Patients (SCC-D)
 - Under "Definition", the following statement was modified: "In these patients, urgent diagnosis and treatment of lesions are important, *and nodal staging (radiologic or pathologic) may be considered in those with significant risk of nodal metastases.*"
 - For treatment of satellite lesions and in-transit metastases, the recommendation to treat aggressively with "strong consideration of radiation therapy as primary therapy" was replaced with "multidisciplinary tumor board consultation."

October 26, 2015

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Melanoma. These NCCN Guidelines® are currently available as Version 1.2016.

- Pathology Report (ME-1)
 - Footnote c revised: "While there is interest in newer prognostic molecular techniques such as gene expression profiling to differentiate *benign from malignant neoplasms*, or melanomas at low- versus high-risk for metastasis, routine (baseline) genetic testing of primary *cutaneous* melanomas (before or following SLNB) is not recommended outside of a clinical study (trial). ~~Mutational analysis is recommended if patients are being considered for either routine treatment or clinical trials, but is not recommended or patients who are otherwise NED.~~"

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- Footnote d is new: "In the absence of metastatic disease, BRAF testing of the primary cutaneous melanoma is not recommended."
- Footnote f revised: "Given lower reported rates of SLN positivity in pure desmoplastic melanoma, it is important that an experienced dermatopathologist examine the entire lesion before making the decision to perform a SLNB. There is uncertainty regarding the diagnostic criteria for, the probability of a positive sentinel node in, and the prognostic significance of the sentinel node in pure desmoplastic melanoma. Multidisciplinary consultation including a dermatopathologist is recommended for determining staging and treatment options. (Busam KJ. Desmoplastic Melanoma. Clin Lab Med 2011;31:321-330.)"
- Clinical Stage
 - Revised the following language:
 - "Stage IA, IB (≤ 0.75 mm thick, any features) no ulceration, mitotic rate 0 per mm^2 ; Stage IB (≤ 0.75 mm thick with ulceration, and/or mitotic rate ≥ 1 per mm^2 ." (ME-2)
 - "Stage IB, Stage II (0.76–1.0 mm thick with ulceration or mitotic rate ≥ 1 per mm^2) or Stage II (>1 mm thick, any characteristic feature, N0)" (ME-3)
- Primary Treatment (ME-4)
 - Recommendation revised, for Stage III (sentinel node positive) disease: "Discuss and offer complete lymph node dissection."
 - Recommendation revised for Stage III (clinically positive node[s]): "...complete therapeutic lymph node dissection."
- Adjuvant Treatment
 - Interferon alfa as an adjuvant treatment option changed from a category 2B to category 2A recommendation for the following stages:
 - Stage III (sentinel node positive) (ME-4)
 - Stage III (clinically positive nodes[s]) (ME-4)
 - Nodal recurrence (ME-9)
 - Biochemotherapy was added as a category 2B recommended adjuvant treatment option for the following stages:
 - Stage III (clinically positive nodes[s]) (ME-4)
 - Nodal recurrence (ME-9)
 - The statement "If free of disease" was divided into two pathways "If free of disease by surgery" and "If free of disease by other treatments". For the latter, "Clinical trial" or "Observation" are recommended as adjuvant treatment options. This change was made for the following settings:
 - After "Primary Treatment" for Stage III in-transit (ME-5)
 - After "Treatment of Recurrence" for local, satellite and/or in-transit recurrence (ME-8)
- Distant Metastatic Disease Workup (ME-10)
 - Revised the following: "FNA (preferred) or lymph node biopsy FNA preferred, if initial resection is planned. Biopsy (core, excisional or incisional) preferred if initial therapy is to be systemic."
- Principles of Radiation Therapy (ME-D)
 - "Adjuvant nodal basin RT is associated with reduced lymph node field recurrence but has no impact on shown no improvement in relapse-free or overall survival. and Its benefits must be weighed against

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potential ~~toxicities~~ the increased probability of long-term skin and regional toxicities and potential reduced quality of life."

- Systemic Therapy For Metastatic or Unresectable Disease (ME-E 1 of 5)
 - This section was reorganized and extensively revised including:
 - The "Metastatic or unresectable disease" treatment pathways for "BRAF V600 wild type" and "BRAF V600 mutant" were combined into one algorithm.
 - Nivolumab/ipilimumab was added to the list of options for "First-line therapy" and "Second-line or subsequent therapy."
 - Footnote 3 is new: *"Nivolumab/ipilimumab combination therapy is associated with improved relapse-free survival compared with single agent nivolumab or ipilimumab, at the expense of significantly increased toxicity. Compared to single agent therapy, the impact of nivolumab/ipilimumab combination therapy on overall survival is not known. The phase III trial of nivolumab alone versus nivolumab/ipilimumab versus ipilimumab alone was conducted in previously untreated patients with unresectable stage III or IV melanoma."*
- Other Systemic Therapies (ME-E 2 of 5)
 - Biochemotherapy for Metastatic Disease
 - This section was extensively revised.
 - New section added, "Biochemotherapy for Adjuvant Treatment of High Risk Disease" with the recommended regimen:
 - "Dacarbazine, cisplatin, vinblastine, IL-2, and interferon alfa-2b (category 2B)."
- Management of Toxicities Associated With Immunotherapy and Targeted Therapy (ME-F)
 - This section was reorganized and extensively revised

October 23, 2015

NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Non-Small Cell Lung Cancer. These NCCN Guidelines® are currently available as Version 1.2016.

- Systemic Therapy for Metastatic Disease; Sensitizing EGFR Mutation Positive (NSCL-17)
 - First-line Therapy
 - EGFR mutation discovered prior to first-line chemotherapy: gefitinib added as a category 1 recommendation.
 - EGFR mutation discovered during first-line chemotherapy: gefitinib added as a treatment option.
 - The option of "May add erlotinib or afatinib to current chemotherapy (category 2B)" removed.
 - Subsequent therapy
 - Gefitinib added as a treatment option for all indications where erlotinib or afatinib are listed.
 - Brain: criteria of "isolated" and "multiple" lesions removed and treatment recommendations consolidated. A link was added to the NCCN Guidelines for CNS Cancer.
 - Multiple lesions: "± erlotinib" removed as a treatment option.
 - Footnote "pp" added: Afatinib + cetuximab may be considered in patients who have progressed on EGFR TKI therapy.

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- Systemic Therapy for Metastatic Disease; ALK Positive (NSCL-18)
 - Subsequent therapy
 - Brain: criteria of “isolated” and “multiple” lesions removed and treatment recommendations consolidated. A link was added to the NCCN Guidelines for CNS Cancer.
- Systemic Therapy for Metastatic Disease; Adenocarcinoma, Large Cell, NSCLC NOS (NSCL-19)
 - PS 0-2
 - Systemic immune checkpoint inhibitors noted as preferred.
 - Pembrolizumab added as a treatment option.
 - Nivolumab changed from a category 2A to a category 1 recommendation.
 - PS 3-4
 - Afatinib and gefitinib added as treatment options for patients with sensitizing EGFR mutations.
 - Crizotinib added as a treatment option for patients with positive ALK rearrangements.
 - Footnote “xx” added: Pembrolizumab is approved for patients with NSCLC tumors with PD-L1 expression, as determined by an FDA-approved test for PD-L1 with use of pembrolizumab.
 - Footnote “bbb” modified: If not already given, options for PS 0-2 include erlotinib, nivolumab, *pembrolizumab*, docetaxel (category 2B), pemetrexed (category 2B), gemcitabine (category 2B), or ramucirumab + docetaxel (category 2B); options for PS 3-4 include erlotinib or best supportive care. Options for further progression are best supportive care or clinical trial.
- Systemic Therapy for Metastatic Disease; Squamous Cell Carcinoma (NSCL-20)
 - PS 0-2
 - Systemic immune checkpoint inhibitors noted as preferred.
 - Pembrolizumab added as a treatment option.
 - Subsequent therapy
 - Erlotinib removed as a treatment option for any performance status.
 - Switch maintenance
 - Erlotinib removed as a treatment option.
 - Footnote “xx” added: Pembrolizumab is approved for patients with NSCLC tumors with PD-L1 expression, as determined by an FDA-approved test for PD-L1 with use of pembrolizumab.
 - Footnote “ccc” modified: If not already given, options for PS 0-2 include ~~erlotinib~~, nivolumab, *pembrolizumab*, docetaxel (category 2B), gemcitabine (category 2B), or ramucirumab + docetaxel (category 2B); options for PS 3-4 include ~~erlotinib~~ or best supportive care. Options for further progression are best supportive care or clinical trial.
 - Footnote removed: Recommend proteomic testing for patients with NSCLC and wild-type EGFR or with unknown EGFR status. A patient with a “poor” classification should not be offered erlotinib in the second-line setting. Gregorc V, Novello S, Lazzari C, et al. Predictive value of a proteomic signature in patients with non-small-cell lung cancer treated with second-line erlotinib or chemotherapy (PROSE): a biomarker stratified, randomised phase 3 trial. *Lancet Oncol* 2014; 15:713-21.
- Emerging Targeted Agents for Patients with Genetic Alterations (NSCL-H)
 - Dabrafenib + trametinib added as an available targeted regimen with activity against BRAF V600E mutation.
 - Cabozantinib changed from a category 2B to a category 2A recommendation.-
 - MET amplification clarified as “High level MET amplification or MET exon 14 skipping mutation”

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NCCN has published updates to the NCCN Drugs & Biologics Compendium (NCCN Compendium®) to reflect updates to the 2016 Version of the corresponding NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®):

- Bone Cancer, V 1.2016

NCCN has published updates to the NCCN Guidelines® and NCCN Compendium® for Uterine Neoplasms. These NCCN Guidelines are currently available as Version 1.2016.

- Global Changes
 - "Serous adenocarcinoma" changed to "Serous *carcinoma*."
 - "Clear cell adenocarcinoma" changed to "Clear cell *carcinoma*."
 - "Stromal mesenchymal tumors" changed to "*Malignant* mesenchymal (*sarcoma*)."
 - "Endometrial stromal sarcoma (ESS)" was divided into "*Low-grade* endometrial stromal sarcoma" and "*High-grade* endometrial stromal sarcoma."
 - "High-grade (undifferentiated) endometrial sarcoma" changed to "*Undifferentiated uterine sarcoma (UUS)*."
- Uterine Neoplasms
 - Footnote "a" revised: "~~Endometrial biopsy is typically not useful in diagnosing malignancies of the uterine wall such as stromal/mesenchymal tumors. Preoperative imaging and biopsy may help to identify uterine sarcomas although biopsy sensitivity is less than for endometrial cancer. If there is suspicion of malignant mesenchymal sarcoma, fragmentation should be avoided.~~" (UN-1)
 - Footnote "b" revised: "... An infrastructure needs to be in place to handle the screening results. IHC and/or MSI screening is usually performed on epithelial tumors ~~and not stromal/mesenchymal endometrial tumors.~~" (UN-1)
 - Principles of Radiation Therapy: A new bullet was added: "*Palliative RT should be individualized to disease extent and patient performance status. Various dose/fractionation schemes can be considered. A common approach is 30 Gy in 10 fractions.*" (UN-A)
- Endometrial Carcinoma
 - Primary treatment
 - For patients with gross cervical involvement who are not suitable for primary surgery (ENDO-2)
 - Recommendation revised: "Tumor-directed *RT ± chemotherapy*." The subsequent recommendation was also revised: "~~Re-evaluate for~~ Surgical resection, *if rendered operable*."
 - A new neoadjuvant "Chemotherapy (category 2B)" pathway was added, followed by re-evaluation for local therapy.
 - For patients with initially unresectable extrauterine pelvic disease (ENDO-3)
 - Recommendation revised: "RT + brachytherapy ± chemotherapy ~~± surgery~~"
 - "*Chemotherapy*" was added as an option, followed by "*Re-evaluate for surgical resection and/or RT based on response*."
 - For patients with extra-abdominal/liver disease (ENDO-3)
 - "Consider palliative TH/BSO ± chemotherapy ± RT ± hormone therapy" changed to "*Chemotherapy and/or RT and/or Hormone therapy*."
 - "May consider palliative TH/BSO" was listed as a separate option.

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- Adjuvant Treatment (ENDO-5)
 - Surgically staged: Stage II, Histologic Grade 2: "Pelvic RT + vaginal brachytherapy" removed as an option and "Vaginal brachytherapy and/or EBRT" was added.
 - Surgically staged: Stage II, Histologic Grade 3: "Pelvic RT + vaginal brachytherapy ± chemotherapy." changed to "EBRT ± vaginal brachytherapy ± chemotherapy."
- Local/regional recurrence (ENDO-10)
 - For patients with extra-vaginal disease in the para-aortic or common iliac lymph nodes after therapy for relapse, recommendation revised: "Tumor-directed RT ± brachytherapy ± chemotherapy."
 - New footnotes added
 - Footnote "t": "May include patients with isolated common iliac or para-aortic lymph node recurrence."
 - Footnote "u": "Consider preoperative EBRT in select patients."
 - Footnote "v": "Post-resection consolidation RT can be considered in patients who were not previously radiated or who are deemed to have additional tolerance for radiation."
- "Serous or clear cell carcinoma or carcinosarcoma of the endometrium": After "Primary Treatment," the "Stage IA" treatment decisions are no longer divided by myometrial invasion. Previously, "Stage IA (with myometrial invasion)" received "Chemotherapy ± tumor-directed RT" (ENDO-11)
- Systemic Therapy for Recurrent, Metastatic, or High-Risk Disease (ENDO-C)
 - Footnote "1" revised: "Hormonal therapy may be used for lower grade endometrioid histologies only (ie, not for G3 endometrioid, serous adenocarcinoma, clear cell adenocarcinoma, or carcinosarcoma) preferably in patients with small tumor volume or an indolent growth pace."
- Uterine Sarcoma
 - "Diagnosed after TH or supracervical hysterectomy ± BSO" pathway: Recommendation revised, "Consider reresection especially if low-grade ESS." (UTSARC-1)
 - Footnote "a" revised: "~~Endometrial biopsy is typically not useful in diagnosing malignancies of the uterine wall such as stromal/mesenchymal tumors. Preoperative imaging and biopsy may help to identify uterine sarcomas although biopsy sensitivity is less than for endometrial cancer. If there is suspicion of malignant mesenchymal sarcoma, fragmentation should be avoided.~~" (UTSARC-1)
 - Footnote removed: "By definition, ESS has low-grade cytologic features. High-grade subtypes of endometrial sarcomas (undifferentiated endometrial sarcomas in WHO classification) are still being defined." (UTSARC-1)
 - High grade ESS was added to the list of Pathologic Findings/Histologic Grades and is treated the same as UUS and uterine leiomyosarcoma. (UTSARC-3)
 - Surveillance (UTSARC-4)
 - Second bullet revised: "~~Consider~~ CT imaging chest/abdomen/pelvis) every 3–6 mo for 2–3 y, then every 6 mo for next 2 y, then annually for high-grade sarcomas."
 - Therapy for Relapse (UTSARC-4)
 - The treatment recommendations for "isolated metastases" and "disseminated disease" were revised extensively.
 - Systemic Therapy for Uterine Sarcoma (UTSARC-A)
 - Eribulin was added as a single agent option.
 - Hormone Therapy: Title revised, "Hormone Therapy (ESS only) (For Low-grade ESS or Hormone Receptor Positive (ER/PR) uLMS)."
 - The categories of evidence and consensus for the following hormone therapies were revised:
 - Medroxyprogesterone acetate (category 2B for ER/PR positive uLMS)

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- Megestrol acetate (*category 2B for ER/PR positive uLMS*)
- GnRH analogs (*category 2B for low-grade ESS and ER/PR positive uLMS*)
- Footnote removed: "Aromatase inhibitors for uLMS that are ER/PR positive."
- Footnote "2" is new: "*These hormonal therapies may be considered for patients with uLMS that is ER/PR positive, preferably with small tumor volume or an indolent growth pace.*"
- Uterine Sarcoma Classification (UTSARC-B)
 - The following uterine sarcoma classifications were revised:
 - *Low-grade endometrial stromal sarcoma (ESS)*
 - *High-grade ESS*
 - ~~High-grade (undifferentiated) endometrial sarcoma~~ *Undifferentiated uterine sarcoma (UUS)*
 - A section listing "Other Rare Uterine Mesenchymal Sarcoma Subtypes" was added.
 - The following footnotes were added:
 - Footnote 2: "*Endometrial stromal sarcomas (LGESS) are characterized by small cells with low-grade cytology and features resembling stromal cells in proliferative endometrium. Mitotic activity is usually low (<5 MF per 10 HPF).*"
 - Footnote 3: "*High-grade endometrial stromal sarcomas (HGESS) are characterized by small cells with high-grade cytology, frequent necrosis, and brisk mitotic activity (>10 MF per 10 HPF). HGESS can contain areas of conventional LGESS.*"
 - Footnote 4: "*Undifferentiated uterine sarcomas (UUS) are characterized by cells with high-grade cytologic features lacking any resemblance to the stromal cells in proliferative endometrium or any other specific type of differentiation.*"

October 19, 2015

NCCN has published **NEW NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)** with NCCN Evidence Blocks™ for the following disease sites:

- Chronic Myelogenous Leukemia, Version 1.2016
- Multiple Myeloma, Version 2.2016

NCCN has published updates to the NCCN Guidelines® for Bone Cancer. These NCCN Guidelines are currently available as Version 1.2016.

- Osteosarcoma
 - For adjuvant treatment, *consider changing chemotherapy* is now a category 2B. (OSTEO-2)
 - Radium 223 dichloride (Ra 223) is new to the page. (OSTEO-4)
- Bone Cancer Systemic Therapy Agents
 - Sorafenib + everolimus added as an option for second-line therapy for relapsed/refractory or metastatic osteosarcoma. (BONE-B)

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NCCN has published updates to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Colorectal. These NCCN Guidelines® are currently available as Version 2.2015.

- The Discussion section has been updated to reflect the changes in the algorithm. (MS-1)

**For your reference, the previous updates (Version 1.2015) to the NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal, published on May 4, 2015, are available at the following link:*

http://www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf

For the complete updated versions of the NCCN Guidelines, NCCN Guidelines with NCCN Evidence Blocks™, NCCN Compendium, and NCCN Templates, please visit NCCN.org.

To access the NCCN Biomarkers Compendium™, please visit NCCN.org/biomarkers.

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