

NCCN Guidelines for Melanoma V.1.2018–Panel Meeting on 06/28/17

Guideline Page and Request	Panel Discussion/References	Vote			
		YES	NO	ABSTAIN	ABSENT
<p><u>ME-1 to ME-3 and ME-B</u> External Submission: Castle Bioscience, Inc request to consider inclusion of the DecisionDx-Melanoma test in the guidelines as a prognostic test that provides risk of metastasis stratification for cutaneous melanoma by revising footnote. Suggest revising footnote to read "...gene expression profiling to differentiate melanomas at low (Class 1) versus high (Class 2) risk for metastasis may provide additional prognostic information beyond standard clinical and pathological staging")"</p>	<p>Based on a review of the data and discussion, the panel voted not to include the revised footnote language proposed in the submission.</p> <p>References: Gerami P, et al. Clin Cancer Res 2015;21:175-183. Gerami P, et al. J Am Acad Dermatol 2015;72:780-785. Berger AC, et al. Curr Med Res Opin 2016;32:1599-1604. Ferris LK, et al. J Am Acad Dermatol 2017;76:818-825.</p>	0	22	2	4
<p><u>ME-4</u> External Submission: Bristol Myers Squibb request to review data presented at the ASCO 2017 Annual Meeting regarding the phase III randomized study that evaluated ipilimumab (3 or 10 mg/kg) versus high-dose interferon alfa-2b for the treatment of patients with resected high-risk melanoma in the adjuvant setting.</p>	<p>After a review of data and discussion, the panel consensus was to wait for full publication of results in a peer-reviewed journal considering. The panel voted to recommend only the high-dose regimen (10 mg/kg) for ipilimumab in the adjuvant setting.</p> <p>Reference: Tarhini AA, et al. J Clin Oncol 2017;35:Abstr 9500.</p>	24	1	0	4
<p><u>ME-8</u> External submission: Foundation Medicine, Inc. request to include comprehensive genomic profiling (CGP), via a single (as opposed to sequential testing) assay, in the initial evaluation of a patient with metastatic melanoma in order to identify <i>BRAF</i> and <i>KIT</i> alterations, other alterations recurrently identified in melanoma such as <i>NRAS</i>, <i>NF1</i>, <i>GNAQ</i>, and <i>GNA11</i>, as well as additional rare driver alterations that may inform the patient's treatment, including the option to enroll in a genomically matched clinical trial. (pages ME-8 through ME-13, ME-B, ME-G)</p>	<p>Based on a review of data and panel member presentation/discussion, the panel supported addressing the submission by adding the following to footnote "hh" on pages ME-8 through ME-14, ME-B, ME-G: "Consider broader genomic profiling if the test results might guide future treatment decisions or eligibility for participation in a clinical trial. " See submission for references.</p>	24	0	0	4

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<p>ME-B External Submission: Myriad Genetic Laboratories, Inc. request to review data and consider inclusion of the myPath Melanoma 23-gene diagnostic expression signature for use as an adjunct to histopathology in the diagnosis of ambiguous melanocytic neoplasms. Make the following changes:</p> <ol style="list-style-type: none"> 1. “Consider use of comparative genomic hybridization (CGH), fluorescence in situ hybridization (FISH), or diagnostic qRT-PCR based 23-gene expression signature for histologically equivocal lesions”. 2. Remove “...to differentiate benign from malignant neoplasms” from footnote 3, along with the corresponding citation. 3. Add the qualifier “prognostic” to the final sentence in footnote 3, i.e. “routine (baseline) prognostic genetic testing of primary cutaneous melanomas (before or following SLNB) is not recommended outside of a clinical study (trial).” 	<p>Principles of Pathology for Primary Melanoma</p> <ol style="list-style-type: none"> 1. Based on a review of the data and discussion, the panel agreed not to include the revised language (point #1) proposed in the submission. However, the panel voted and agreed to use the following language to address the submission: “Consider the use of comparative genomic hybridization (CGH) or fluorescence in situ hybridization (FISH) molecular testing for histologically equivocal lesions.” 	24	1	0	3
	<ol style="list-style-type: none"> 2. Based on a review of data, and discussion, the panel voted to use the revised language proposed in the submission (points #2 and #3) for footnote “3” as follows: “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) prognostic genetic testing of primary cutaneous melanomas (before or following sentinel lymph node biopsy [SLNB]) is not recommended outside of a clinical study (trial).” <p>See submission for references.</p>	22	1	1	4
<p>ME-G 1 of 6 External Submission: Bristol-Myers Squibb Company request to review data presented at the AACR Annual Congress and consider amending footnote 5 as follows: “...Compared to single-agent therapy, the impact of nivolumab/ipilimumab combination therapy on overall survival is not known. The phase III trial of nivolumab/ipilimumab or nivolumab monotherapy versus ipilimumab monotherapy was conducted in previously untreated patients with unresectable stage III or IV melanoma.”</p>	<p>Based on a review of data, the panel discussed that anti PD-1 monotherapy is generally preferred over nivolumab/ipilimumab because of the substantial increase in toxicity of the combination therapy without a substantial increase in response rate. To address the submission and institutional review comments the following changes were made to footnote “5”: “Nivolumab/ipilimumab combination therapy is associated with improved ORR and PFS 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/ipilimumab or nivolumab monotherapy versus either nivolumab or ipilimumab monotherapy was conducted in previously untreated patients with unresectable stage III or IV melanoma.”</p> <p>Reference: Larkin J, et al. N Engl J Med 2015;373:23-34.</p>	22	0	0	6

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<p>ME-G 1 of 6</p> <p>External submission: Merck & Co. request to consider the addition of pembrolizumab as a systemic treatment option for adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors that has progressed following prior treatment and who have no satisfactory alternative treatment options.</p>	<p>The NCCN Guidelines for Melanoma do not include recommendations for pediatric patients. Based on a review of data and discussion, the panel noted that pembrolizumab is currently listed as an option for second-line or subsequent therapy for metastatic or unresectable disease. The panel supported not expanding the recommendation further.</p> <p>See submission for references.</p>	0	22	2	4
<p>ME-G 1 of 6</p> <p>Institutional review comment: Discuss the role of biochemotherapy and consider removing it as an option for treating metastatic or unresectable disease.</p>	<p>Based on a review of data and discussion of clinical practice at member institutions, the panel voted to remove biochemotherapy as a second-line or subsequent therapy option for treating metastatic or unresectable disease.</p> <p>References: Eton O, et al. J Clin Oncol 2002;20:2045-2052. Atkins MB, et al. J Clin Oncol 2008;26:5748-5754. Ives NJ, et al. J Clin Oncol 2007;25:5426-5434.</p>	16	6	1	5