

NCCN Guidelines for Cutaneous Melanoma V.1.2021– Annual on 07/13/20

Guideline Page and Request	Panel Discussion/References	Vote			
		YES	NO	ABSTAIN	ABSENT
<p>ME-1 External request: Submission from Myriad (06/09/20) Request to add a third arrow in the flow chart from “Biopsy” to “Melanoma not confirmed” with a new footnote reading: “If melanoma not confirmed, review risk factors, including consideration of multigene panel testing for hereditary risk, and counsel patient on strategies for melanoma prevention and screening. See Risk Factors for Melanoma Development (ME-A) and Common Follow-up Recommendations for All Patients (ME-11).”</p>	<p>Based on a review of the data and discussion, the panel consensus was not to make changes to the current recommendations within the guidelines.</p> <p>See Submission for references.</p>	0	28	0	3
<p>ME-7 Internal request: Institutional review comment to consider removing “BCG or IL-2” as intralesional options for unresectable stage III (clinical satellite/in-transit) disease.</p>	<p>Based on the review of the data, the panel consensus was to remove BCG as an option for unresectable stage III (clinical satellite/in-transit) disease and for unresectable local satellite/in-transit recurrent disease due to limited clinical use in these settings.</p>	28	0	0	3
<p>ME-16 and ME-I External request: Submission from Merck and Co (01/13/20) Request that the NCCN panel consider the inclusion of pembrolizumab in combination with bevacizumab as a treatment option for patients with disseminated (unresectable) melanoma with brain metastases in the appropriate sections of the guidelines, including sections ME-15 and ME-I.</p>	<p>Based on a review of the data and discussion, the panel consensus did not support the inclusion of pembrolizumab in combination with bevacizumab as an option due to data provided was based on an abstract reporting on a small study. The panel will wait for publication of data from larger trial for further review of the data.</p> <p>See Submission for references.</p>	0	28	0	3

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<p>ME-A External request: Submission from Myriad (06/09/20) Risk Factors for Development of Single or Multiple Primary Melanomas, under “Genetic predisposition”:</p> <ul style="list-style-type: none"> • Add <i>TERT</i>, <i>MITF</i> and <i>PTEN</i> to the list of genes predisposing to melanoma in the first sub-bullet. • Add renal and breast cancer to the list of relevant family history malignancies and add citation 3 for the second sub-bullet. 	<p>Based on a review of the data and discussion, the panel consensus supported the inclusion of the noted gene mutations and cancers as follows:</p> <ul style="list-style-type: none"> • First arrow sub-bullet revised: Presence of germline mutations or polymorphisms predisposing to melanoma (including eg, <i>CDKN2a</i>, <i>CDK4</i>, <i>MC1R</i>, <i>BRCA2</i>, <i>BAP1</i> [especially for uveal melanoma], <i>TERT</i>, <i>MITF</i>, <i>PTEN</i> and potentially <i>potential</i> other genes). • Second arrow sub-bullet revised: Family history of cutaneous melanoma (especially if multiple), pancreatic cancer, renal and/or breast cancer, astrocytoma, uveal melanoma, and/or mesothelioma. <p>See Submission for references.</p>	28	0	0	3
<p>ME-C (5 of 7) External request: Submission from Foundation Medicine, Inc. (06/22/20 and 09/15/20) Under “Somatic mutation burden”</p> <ul style="list-style-type: none"> • Amend sub-bullet point 3 to include the following: tumor mutational burden (TMB) measured and reported by targeted NGS panels should be validated and/or FDA-approved per the recommendations outlined by the Friends of Cancer Research TMB Harmonization Project. • Remove last diamond sub-bullet: “The use of mutation burden to guide treatment decisions remains investigational at this time.” 	<p>Based on a review of the data and discussion, the panel consensus was not to make changes to the current recommendations.</p> <p>See Submission for references.</p>	0	28	0	3

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		YES	NO	ABSTAIN	ABSENT
<p>ME-I (1 of 8) External request: Submission from Merck & Co (06/16/20) Request the inclusion of pembrolizumab in combination with low-dose ipilimumab as a second-line or subsequent treatment option for patients with confirmed progression of unresectable or metastatic melanoma after treatment with an anti-PD1 antibody in the appropriate sections of the NCCN Cutaneous Melanoma Guidelines, including ME-I.</p>	<p>Based on the review of the data in the noted reference, the panel consensus was to include pembrolizumab/low-dose ipilimumab for tumors that have progressed after prior anti-PD-1 therapy as a second-line treatment option. This is a category 2A (preferred) recommendation. The following corresponding footnotes were also added</p> <ul style="list-style-type: none"> • See NCCN Guidelines for Management of Immunotherapy-Related Toxicities for proactive monitoring and management of toxicities in patients undergoing treatment with immune checkpoint inhibitors. • Testing for tumor PD-L1 should not guide clinical decision-making. The utility of this biomarker requires further investigation. <p><u>Reference</u></p> <ul style="list-style-type: none"> • Olson DJ, Luke JJ, Poklepovic AS, et al. Significant antitumor activity for low-dose ipilimumab (IPI) with pembrolizumab (PEMBRO) immediately following progression on PD1 Ab in melanoma (MEL) in a phase II trial. Presented at: American Society of Clinical Oncology (ASCO) 2020 Virtual Scientific Program; J Clin Oncol 2020;38(suppl);abstr 10004. 	28	0	0	3

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<p>ME-J External requests</p> <ul style="list-style-type: none"> • Submission from Merck & Co. (04/29/20) requesting the inclusion of the updated dosing recommendations for pembrolizumab, either 200 mg every 3 weeks or 400 mg every 6 weeks administered as a 30-minute intravenous (IV) infusion: <ul style="list-style-type: none"> ○ until disease progression or unacceptable toxicity for the treatment of adult patients with unresectable or metastatic melanoma, to pages ME-J (1 of 4), MS-50, and MS-52 in the NCCN Cutaneous Melanoma Guidelines. ○ until disease recurrence, unacceptable toxicity, or up to 12 months for the adjuvant treatment of adult patients with melanoma to pages, ME-J (1 of 4), MS-50, and MS-52 in the NCCN Cutaneous Melanoma Guidelines. • Submission from Value in Cancer Care Consortium (Vi3C) (03/01/20; 06/10/20) Request to amend the NCCN guidelines to include the option of weight-based dosing of pembrolizumab (2 mg/kg every three weeks or 4 mg/kg every 6 weeks) as alternative options to fixed dosing (200mg every 3 weeks or 400 mg every 6 weeks). 	<p>Based on a review of the data and discussion, the panel consensus was to modify the “Considerations for Selection of Systemic Therapy for Unresectable or Metastatic Disease” section by adding a new sub-bullet to the Considerations for anti-PD-1/ipilimumab dosing and anti-PD-1 monotherapy dosing” bullet as follows: <i>The initial clinical trials and FDA approvals of pembrolizumab and nivolumab in 2014 used dosing based on patient weight (2 mg/kg every 3 weeks for pembrolizumab and 3 mg/kg every 2 weeks for nivolumab). Subsequently the FDA amended dosing to flat doses (200 mg or 400 mg every 3 or 6 weeks, respectively, for pembrolizumab, or 240 mg or 480 mg every 2 or 4 weeks, respectively, for nivolumab), which are safe and efficacious. However, substantial cost savings for pembrolizumab and nivolumab may be obtained by weight-based dosing, depending on patient weight and on institutional practices regarding vial sharing.</i></p> <p>See Submissions for references.</p>	28	0	0	3