

**Please note: This update does not include all of the submissions received. Those not listed below will included in the Version 1.2018 update of the NCCN Guidelines for Breast Cancer.**

Guideline Page and Request	Panel Discussion/References	Institution Vote			
		YES	NO	ABSTAIN	ABSENT
<p>BINV-5, BINV-13, and BINV-15  <u>Internal request:</u>                      Discuss addition of extended HER2 targeted therapy with neratinib.</p> <p><u>External request from Puma Biotechnology, Inc.:</u>                      Please consider the available data on the use of neratinib for the extended adjuvant treatment of adult patients with early-stage, HER2+ BC following treatment with adjuvant trastuzumab therapy.</p>	<p>Based upon Panel discussion and review of the data in the noted references, the Panel supported adding the following footnote to the guidelines:                      “Consider extended adjuvant neratinib following adjuvant trastuzumab-containing therapy in HR-positive patients with a perceived high risk of recurrence (such as stage II-III). The benefit or toxicities associated with extended neratinib in patients who have received pertuzumab is unknown.”  <a href="#">See Submission for references</a></p>	17	2	2	7
<p>BINV-5, BINV-7, BINV-13 and BINV-15  <u>Internal request:</u></p> <ul style="list-style-type: none"> <li>• Discuss whether to add recommendations for adjuvant pertuzumab.</li> <li>• Consider in which settings one full year of adjuvant pertuzumab should be included.</li> </ul> <p><u>External request from Genentech, Inc.:</u>                      Consider the Phase 3 APHINITY trial results for your evaluation of adjuvant pertuzumab, trastuzumab and chemotherapy in patients with operable HER2-positive EBC.</p>	<p>Based upon Panel discussion and review of the data in the noted references, the panel consensus was to include adjuvant pertuzumab for node positive, HER2-positive tumors. This is a category 2A recommendation. The panel also included the dose/schedule on BINV-K.</p> <p><a href="#">See Submission for references</a></p> <p>Von Minckwitz G., Procter M., Azambuja E., et al. Adjuvant pertuzumab and trastuzumab in early HER2-positive breast cancer. N Engl J Med 2017; 377:122-131.  <a href="#">von Minckwitz G et al. NEJM 2017 June 5 [Epub ahead of print]</a></p>	23	0	0	5
<p>BINV-13 and BINV-15  <u>Internal requests:</u></p> <ul style="list-style-type: none"> <li>• Consider inclusion of the CREATE-X data for post-neoadjuvant therapy of HER2 negative breast cancer with residual disease at surgery.</li> <li>• For which patients should post-neoadjuvant capecitabine be considered?</li> </ul>	<p>Based upon Panel discussion and review of the data in the noted reference, the Panel supported adding the following recommendation to the guidelines:                      “Consider adjuvant capecitabine in patients with triple-negative breast cancer and residual invasive cancer following standard neoadjuvant treatment with taxane-, alkylator- and anthracycline-based chemotherapy.”</p> <ul style="list-style-type: none"> <li>• Masuda N, Lee SJ, Ohtani S, et al. Adjuvant capecitabine for breast cancer after preoperative chemotherapy. N Engl J Med 2017;376:2147-2159.  <a href="#">Masuda et al. NEJM 2017;376:2147-2159</a></li> </ul>	22	1	0	5

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<p>BINV-16  <u>External request from ImpediMed, Inc.:</u>                      Request to expand, “educate, monitor, and refer for lymphedema management” to read:                      Provide education on risk of lymphedema and risk reduction practices; monitor for early stage lymphedema using an objective, reproducible tool, such as bioimpedance spectroscopy (BIS); and refer for early lymphedema management.</p>	<p>Based upon Panel discussion and review of the current guideline recommendations, the panel did not support expanding the recommendation.</p>	0	23	0	5
<p>BINV-17  <u>External request from Myriad Genetic Laboratories, Inc.:</u>                      Add a bullet to list under “Determination of ER/PR and HER2 status on metastatic site.” New bullet to be: “Determine <i>BRCA</i> status to establish eligibility for treatment with a PARP inhibitor.”                      Add footnote: “Patients with a <i>BRCA</i> mutation experience extended progression free survival on PARP inhibitor therapy over standard chemotherapy.”</p>	<p>Based upon Panel discussion and review of the data in the noted references, the Panel did not support adding this request.                      However, the panel added a footnote for Olaparib on BINV-O stating: “Patients with HER2-negative disease eligible for single-agent therapy are eligible for germline <i>BRCA</i> 1/2 testing”   <a href="#">See Submission for references</a></p>	0	23	1	4
<p>BINV-K  <u>Internal request:</u>                      Consider removing FEC-based chemotherapy regimen options from the Preoperative/Adjuvant Therapy setting.</p>	<p>Panel consensus supported removing these regimens.</p>	20	0	2	6
<p>BINV-20 and BINV-N  <u>Internal request:</u></p> <ul style="list-style-type: none"> <li>Consider adding option of combining palbociclib with all aromatase inhibitors in metastatic ER-positive, HER2-negative breast cancer setting.</li> </ul> <p><u>External request from Pfizer, Inc.</u>                      The recommended change is to update the NCCN Guidelines to list the combination of palbociclib with an aromatase inhibitor as first line endocrine therapy for recurrent or stage IV disease in postmenopausal patients.</p>	<p>Based upon Panel discussion and review of the data in the noted references, the Panel supported adding palbociclib in combination with an aromatase inhibitor as a treatment option for postmenopausal women with hormone receptor-positive, HER2-negative metastatic breast cancer. This is a category 1 recommendation.   <a href="#">See Submission for references</a></p>	20	0	2	6

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<p>BINV-20 and BINV-N  <u>Internal request:</u></p> <ul style="list-style-type: none"> <li>Consider adding option of combining ribociclib with all aromatase inhibitors in metastatic, hormone positive, HER2-negative breast cancer setting.</li> </ul> <p><u>External request from Novartis Pharmaceutical Corp.</u>  The recommended change is to update the NCCN Guidelines to list ribociclib in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women with hormone receptor positive, HER2 negative advanced or metastatic breast cancer.</p>	<p>Based upon Panel discussion and review of the data in the noted references, the Panel supported adding ribociclib in combination with an aromatase inhibitor as a treatment option for postmenopausal women with hormone receptor-positive, HER2-negative metastatic breast cancer. This is a category 1 recommendation.</p> <p><a href="#">See Submission for references</a></p>	20	0	2	6
<p>BINV-20 and BINV-N  <u>External request from AstraZeneca.</u>  Suggest increasing the level of evidence available for fulvestrant as an initial monotherapy option in patients who are HR+. Furthermore, for the footnotes associated with fulvestrant, we suggest including data from the FALCON and FIRST studies which demonstrated significant progression free survival (PFS) and time to progression (TTP) improvement with fulvestrant versus anastrozole, respectively.</p> <p>On page MS-55, we recommend including the FALCON study results indicated below and an update to the last sentence in column 1, paragraph 1 to read, "In a prospective Phase III trial, the benefit of fulvestrant over anastrozole as initial therapy has been confirmed."</p>	<p>Based upon Panel discussion and review of the data in the noted references, the Panel supported changing the NCCN Category of Evidence and Consensus from a category 2A to a category 1.</p> <p>The updates to the Discussion section will be made at the time of updating the Discussion.</p> <p><a href="#">See Submission for references</a></p>	23	0	0	5
<p>BINV-N  <u>External request from Novartis Pharmaceutical Corp.</u>  Recommend that everolimus in combination with fulvestrant be included as an option for postmenopausal women with hormone receptor positive, HER2-negative metastatic breast cancer resistant to aromatase inhibitor therapy and update relevant discussion section.</p>	<p>Based upon Panel discussion and review of the data in the noted references, the Panel supported adding everolimus in combination with fulvestrant as a treatment option for postmenopausal women with hormone receptor-positive, HER2-negative metastatic breast cancer.</p> <p><a href="#">See Submission for references</a></p>	16	4	3	5

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<p>BINV-N  <u>Internal request</u>                  Recommend everolimus in combination with tamoxifen be included as an option for postmenopausal women with hormone receptor positive, HER2-negative metastatic breast cancer.</p>	<p>Based upon Panel discussion and review of the data, the Panel supported adding everolimus in combination with tamoxifen as a treatment option for postmenopausal women with hormone receptor-positive, HER2-negative metastatic breast cancer.</p>	16	4	3	5
<p>BINV-N  <u>External request from Eli Lilly and Company</u>                  Request review of data and consider abemaciclib in the NCCN Breast Cancer Guidelines in combination with fulvestrant in hormone receptor positive, HER2-negative, metastatic breast cancer.</p>	<p>Based upon Panel discussion and review of the data in the noted references, the Panel supported adding abemaciclib in combination with fulvestrant as a treatment option for postmenopausal women with hormone receptor-positive, HER2-negative metastatic breast cancer, with a footnote. This is a category 1 recommendation.</p> <p>The footnote: “Indicated after progression on prior endocrine therapy in the metastatic setting.”</p>	21	0	3	4
<p>BINV-N  <u>External request from Eli Lilly and Company</u>                  Request review of data and consider abemaciclib in the NCCN Breast Cancer Guidelines as monotherapy in hormone receptor positive, HER2-negative, metastatic breast cancer.</p>	<p>Based upon Panel discussion and review of the data in the noted references, the Panel supported adding abemaciclib monotherapy as a treatment option for postmenopausal women with hormone receptor-positive, HER2-negative metastatic breast cancer, with a footnote. This is a category 2A recommendation.</p> <p>The footnote: “Indicated after progression on prior endocrine therapy and prior chemotherapy in the metastatic setting.”</p>	20	1	3	4

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<p><b>BINV-O</b>  <u>Internal requests:</u></p> <ul style="list-style-type: none"> <li>• Please consider whether to include olaparib as a treatment option for metastatic HER2-negative breast cancer in the setting of a germline <i>BRCA</i> mutation.</li> <li>• Add olaparib as a treatment option for g<i>BRCA</i>1/2 metastatic breast cancer.</li> <li>• Discuss olaparib (Olympia trial).</li> </ul> <p><u>External request from AstraZeneca.</u>                  Consider appropriate inclusion of the OlympiAD data in the Breast Cancer Guidelines. OlympiAD evaluated olaparib monotherapy versus standard of care chemotherapy in patients with germline <i>BRCA</i> mutations and human epidermal growth factor receptor-2 (HER2)-negative metastatic breast cancer, who had received <math>\leq 2</math> lines of chemotherapy in the metastatic setting.</p> <p><u>External request from Myriad Genetic Laboratories, Inc.</u>                  Add olaparib monotherapy to “Other single agents,” with a footnote specifying this therapy is only appropriate for ER/PR positive, HER2-negative patients with a <i>BRCA</i>1 or <i>BRCA</i>2 mutation.</p>	<p>Based upon Panel discussion and review of the data in the noted references, the Panel supported adding olaparib as a treatment option for HER2-negative, <i>BRCA</i> 1/2-positive tumors with the following footnote:                  “Patients with HER2-negative disease eligible for single-agent therapy are eligible for germline <i>BRCA</i> 1/2 testing.”</p> <p>Robson M, Im S, Senkus E, et al. Olaparib for metastatic breast cancer in patients with a germline <i>BRCA</i> mutation. <i>N Engl J Med</i> 2017; 377:523-533</p> <p><a href="#">See Submissions for references</a></p>	21	2	1	4
<p><u>External request from Merck &amp; Co.</u>                  Recommend 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>Based upon Panel discussion and review of the data in the noted references, the Panel did not support the request noted.  <a href="#">See Submissions for references</a></p>	23	0	0	5
<p><u>External request from Celgene Corporation</u>                  Recommend the use of albumin-bound paclitaxel in combination with carboplatin for recurrent or metastatic breast cancer, with a Category 2A recommendation, based on results from the Phase II randomized tenacity trial in patients with TNMBC.</p>	<p>Based upon Panel discussion and review of the data in the noted references, the Panel did not support the request noted.  <a href="#">See Submissions for references</a></p>	23	0	0	5

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<p><u>External request from American Society for Radiation Oncology</u>                  Recommend clarification on the locoregional recurrence section of the Breast Guideline reading “no prior RT, but consider re-irradiation if it can be safely administered.”</p>	<p>The NCCN Radiation Compendium was updated to reflect the change requested.</p>	na	na	na	na
<p><u>External request from Hadassah-Hebrew University Medical Center</u>                  Review “Final 10-year results of Breast International Group 2-98 phase III trial and the role of Ki67 in predicting benefit of adjuvant docetaxel in patients with oestrogen receptor positive breast cancer.” for inclusion in the adjuvant taxane chemotherapy recommendation of breast cancer.</p>	<p>Based upon Panel discussion and review of the data in the noted references, the Panel did not support the request noted.  <a href="#">See Submissions for references</a></p>	23	0	0	5
<p><u>External request from TerSera Therapeutics.</u>                  Clarify that goserelin is the only FDA-approved LHRH agonist for the management of breast cancer in the Adjuvant Endocrine Therapy discussion. Clarify that leuprolide is not FDA-approved for breast cancer</p>	<p>Based upon Panel discussion and review of the data in the noted references, the Panel did not support the request noted.  <a href="#">See Submissions for references</a></p>	23	0	0	5