Guideline Page and Request	Panel Discussion/References	Institution Vote			
		YES	NO	ABSTAIN	ABSENT
BINV-5, BINV-6, and BINV-9 Internal request from Institutional review: • Consider adjuvant use of bisphosphonates in postmenopausal women with ER-positive breast cancer. External request: Submission from Sylvester Comprehensive Cancer Center/University of Miami Hospital and Clinics. Specific recommended changes to the NCCN Breast Cancer Guidelines: • Recommend the use of zoledronic acid in the adjuvant setting in the treatment of breast cancer.	Based on the data in the noted references and discussion, the NCCN Panel consensus was to include a footnote. "Consider adjuvant bisphosphonate therapy in postmenopausal (natural or induced) patients receiving adjuvant endocrine therapy." See Submission for references.	24	0	0	3
BINV-6 and BINV-J External request: Submission from Biotheranostics, Inc. Specific recommended changes to the NCCN Breast Cancer Guidelines: • Addition of BCI for patients with node-negative, HR+ tumors ≥0.5cm, as a complementary gene expression-based prognostic test, to aid in individualized decision-making for EET following completion of adjuvant endocrine treatment. The specific request is a component or footnote of the clinical guideline as follows: "The Breast Cancer Index prognostic multigene assay may be considered to help assess residual risk of late distant recurrence (post 5 year) after completion of adjuvant endocrine therapy."	The NCCN Panel consensus was to defer this request to the next update in order to have a more detailed discussion. See Submission for references.	24	0	0	3

BINV-6 External request: Submission from Genomic Health, Inc. Specific recommended changes to the NCCN Breast Cancer Guidelines: • Recommend the Oncotype DX Breast Cancer Assay as a component of the treatment guideline for HER-2 negative, ER-positive tumors (BINV-6) as an additional bullet (Proposed bullet: The panel recommends the Oncotype DX Breast Cancer Assay for patients with 1-3 node positive, ER-positive, HER-2 negative early stage breast cancer to inform the individualized adjuvant treatment decision).	The NCCN Panel consensus was to defer this request to the next update in order to have a more detailed discussion. See Submission for references.	24	0	0	3
BINV-6 External request: Submission from Genomic Health, Inc. Specific recommended changes to the NCCN Breast Cancer Guidelines: • The Oncotype DX Invasive Breast Cancer Assay language to be changed from “consider” to “recommend” in the N0 and pN1mic (micrometastases) component of the invasive breast cancer algorithm.	The NCCN Panel consensus was to defer this request to the next update in order to have a more detailed discussion. See Submission for references.	24	0	0	3
BINV-6 External request: Submission from NanoString Technologies, Inc. Specific recommended changes to the NCCN Breast Cancer Guidelines: • We request to modify the decision tree/treatment algorithm by including the PAM50 gene signature assay in assessing the risk of recurrence and selection of adjuvant therapy, or alternatively, recommend only a footnote “dd” without highlighting any specific assay(s) in the decision tree/treatment algorithm.	The NCCN Panel consensus was to defer this request to the next update in order to have a more detailed discussion. See Submission for references.	24	0	0	3

BINV-6 and BINV-J External request: Submission from Myriad Genetic Laboratories, Inc. Specific recommended changes to the NCCN Breast Cancer Guidelines: • For tumors >0.5cm replace “consider 21-gene RT-PCR assay” with “consider use of a breast tumor biomarker assay”. Remove specific scores from guidelines but keep categories. To footnote dd, add “21-gene RT-PCR assay, 12-gene risk score (EndoPredict), PAM50 and Breast Cancer Index have been validated as prognostic markers for this use”. • Add 12-gene risk score (EndoPredict) to footnote cc as appropriate for use in patients with node-positive disease. • On BINV-J (adjuvant endocrine therapy) add footnote “Consider use of 21-gene RT-PCR assay, 12-gene risk score (EndoPredict), PAM50 or Breast Cancer Index to identify patients who will likely not benefit from extended adjuvant endocrine therapy”.	The NCCN Panel consensus was to defer this request to the next update in order to have a more detailed discussion. See Submission for references.	24	0	0	3

BINV-16 External request: Submission from Amgen, Inc. Specific recommended changes to the NCCN Breast Cancer Guidelines • 8th Bullet: Women on an aromatase inhibitor or who experience ovarian failure secondary to treatment should have monitoring of bone health with a bone mineral density determination at baseline and periodically thereafter *discuss treatment options to maintain or to improve bone mineral density*. • Footnote pp: The use of estrogen, progesterone, or selective estrogen receptor modulators to treat osteoporosis or osteopenia in women with breast cancer is discouraged. *Adjuvant denosumab 60mg administered every 6 months significantly reduced the risk of clinical fractures in postmenopausal women with breast cancer receiving an aromatase inhibitor for up to 7 years. This effect was observed in women with both normal (T-score ≥ -1.0) and abnormal (T-score < -1.0) bone mineral density at initiation of therapy.* The use of a bisphosphonate or denosumab is acceptable to maintain or to improve bone mineral density. Optimal duration of either therapy has not been established. *The potential benefits of duration of bisphosphonate therapy* beyond 3 y is not known	Based on the data in the noted references and discussion, the NCCN Panel consensus was to modify the footnote. "The use of estrogen, progesterone, or selective estrogen receptor modulators to treat osteoporosis or osteopenia in women with breast cancer is discouraged. The use of a bisphosphonate ***(oral/IV) or denosumab is acceptable to maintain or*** to improve bone mineral density ***and reduce risk of fractures in postmenopausal (natural or induced) patients receiving adjuvant endocrine therapy***. Optimal duration of ***either*** therapy has not been established. ***Duration beyond 3 y is not known***. Factors to consider for duration of anti-osteoporosis therapy include bone mineral density, response to therapy, and risk factors for continued bone loss or fracture. Women treated with a bisphosphonate ***or denosumab*** should undergo a dental examination with preventive dentistry prior to the initiation of therapy, and should take supplemental calcium and vitamin D." See Submission for references.	24	0	0	3
BINV-19 External request: Submission from Amgen, Inc. Specific recommended changes to the NCCN Breast Cancer Guidelines and corresponding Evidence Blocks: • Footnote zz: Denosumab, zoledronic acid, or pamidronate (all with calcium and vitamin D supplementation) should be given (category 1) in addition to chemotherapy or endocrine therapy if bone metastasis is present, expected survival is ≥3 months, and renal function is adequate *with use of a bisphosphonate. In a single phase 3, randomized,*	The NCCN Panel consensus did not support recommendation for change in the NCCN Breast Cancer Guidelines nor corresponding Evidence Blocks. See Submission for references.	24	0	0	3

active-controlled trial, denosumab demonstrated superiority to zoledronic acid in delaying time to first on-study SRE and time to first-and-subsequent on-study SREs in patients with breast cancer and bone metastases and did not require dose modification for renal impairment. Patients should undergo a dental examination with preventive dentistry prior to initiation of this therapy. ~~The optimal schedule~~ *For* zoledronic acid, *the optimal schedule* is monthly x 12, *and then quarterly; for denosumab, the optimal schedule is once every 4 weeks.*					
BINV-20 and BINV-N Internal request from Institutional review: • Request palbociclib + letrozole change to a category 1 option with PALOMA2 data.	Based on the data in the noted reference and discussion, the NCCN Panel consensus supported changing the recommendation to a category 1. Finn RS, Martin M, Rugo HS, et al. Palbociclib and Letrozole in Advanced Breast Cancer. N Engl J Med 2016;375:1925-1936. http://www.nejm.org/doi/full/10.1056/NEJMoa1607303	17	0	0	9
BINV-J Internal request from Institutional Review: Revise option for adjuvant endocrine therapy to include up to 10 years of an aromatase inhibitor.	Based on the data in the noted reference and discussion, the NCCN Panel consensus supported revising the recommendation to "Consider aromatase inhibitor for an additional 5 y." Goss PE, Ingle JN, Pritchard KI, et al. Extending aromatase-inhibitor adjuvant therapy to 10 years. N Engl J Med. 2016 July 21;375(3):209-19. https://www.ncbi.nlm.nih.gov/pubmed/27264120	24	0	0	3
BINV-K External request: Submission from Celgene Corp. Specific recommended changes to the NCCN Breast Cancer Guidelines: • We respectfully request the Panel's consideration for an update to the current Guidelines surrounding Preoperative/Adjuvant Therapy for breast cancer to include albumin-bound paclitaxel as a neoadjuvant induction regimen prior to consolidation at a dose of 125 mg/m2 dosed weekly for 12 consecutive weeks to reflect recently published results from two Phase III studies in	Based on the data in the noted references and discussion, the NCCN Panel consensus was to modify the footnote. "Nab-paclitaxel may be substituted for paclitaxel or docetaxel due to medical necessity (i.e., hypersensitivity reaction). If substituted for weekly paclitaxel or docetaxel, then the weekly dose of nab-paclitaxel should not exceed 125 mg/m^2." See Submission for references.	23	1	2	1

early breast cancer: the GeparSepto trial and the ETNA trial.					
BINV-K Internal request: Remove the following regimens: • FEC/CEF followed by T (fluorouracil/epirubicin/cyclophosphamide followed by docetaxel) or (fluorouracil/epirubicin/cyclophosphamide followed by weekly paclitaxel) • FAC followed by T (fluorouracil/doxorubicin/cyclophosphamide followed by weekly paclitaxel)	Based on the data in the noted references and discussion, the NCCN Panel supported removing these regimens. Del Mastro L, De Placido S, Bruzzi P, et al. Fluorouracil and dose-dense chemotherapy in adjuvant treatment of patients with early-stage breast cancer: an open-label, 2 x 2 factorial, randomised phase 3 trial. Lancet 2015;385:1863-1872. https://www.ncbi.nlm.nih.gov/pubmed/25740286				
BINV-L External request: Submission from Genentech, Inc. Specific recommended changes to the NCCN Breast Cancer Guidelines: • In the current guidelines, the potential benefits of preoperative HER2-targeted therapy for HER2-positive patients are elaborated in section BINV-L [Principles of Preoperative Systemic Therapy] and included as footnote “jj” on page BINV-12. At this critical time point of care before surgery, a clinician may overlook the footnote and the potential benefit of HER2 testing and the option of HER2-targeted therapy because neither are stated explicitly on page BINV-12. As such, please consider the addition of explicit verbiage regarding the option of preoperative HER2-targeted therapy for HER2-positive patients alongside the consideration of endocrine therapy on page BINV-12. Specific language will make this information more consistent with the level of detail that presents endocrine therapy and will help clinicians be more informed of beneficial treatment options prior to surgery.	Based on discussion, the NCCN Panel consensus did not support a change to the guidelines. See Submission for references.	24	0	0	3
BINV-N External request: Submission from Pfizer, Inc. Oncology. Specific recommended changes to the NCCN Breast Cancer Guidelines: • Modify footnote: For postmenopausal women or premenopausal women receiving ovarian suppression with an LHRH agonist with hormone receptor positive	The NCCN Panel consensus supported changing the language in the footnote as requested. See Submission for references.	24	0	0	3

and HER2 negative metastatic breast cancer that has progressed *on or after prior adjuvant or metastatic endocrine therapy*.					
BINV-O, page 1 External request: Submission from Celgene Corp. Specific recommended changes to the NCCN Breast Cancer Guidelines with Evidence Blocks: • We conducted a review of the recently released NCCN Evidence Blocks for MBC in relation to the evidence for albumin-bound paclitaxel in MBC. Considering the NCCN definitions for the Evidence Blocks ratings, and based on the supporting evidence described in the rationale section below, we request NCCN to reevaluate the efficacy rating for albumin-bound paclitaxel in MBC.	The NCCN Panel re-evaluated the efficacy rating for albumin-bound paclitaxel in MBC. It was changed from a 3 to a 4. See Submission for references.	16	0	0	11
BINV-N External request: Submission from Novartis Pharmaceuticals Corp. Specific recommended changes to the NCCN Breast Cancer Guidelines with Evidence Blocks: • Please consider the data related to the stomatitis safety profile, including patient-reported outcomes, with concomitant dexamethasone oral solution and everolimus + exemestane when assessing the overall safety of everolimus in the treatment of metastatic HR+/HER2- breast cancer.	No change was requested, submission for information purposes only. See Submission for references.	NA	NA	NA	NA
MS-44 External request: Submission from Merck & Co., Inc.: • Request that pembrolizumab be added as immunotherapy for systemic therapy in patients with advanced triple negative breast cancer in the Discussion section.	The data submitted are results of phase Ib trial and since immunotherapy is currently not included in the algorithms, it was decided that this should not be included in the Discussion section at the present time. See Submission for references.	NA	NA	NA	NA