Guideline Page and Request	Panel Discussion/References	Institution Vote			
		YES	NO	ABSTAIN	ABSENT
DCIS-1 External request from Genomic Health, Inc. Request the NCCN Breast Cancer Guideline Panel to review the data for inclusion of the 12-gene Oncotype DX® Breast DCIS Score™ assay in the initial work-up for patients diagnosed with DCIS, to stratify patients by risk of local recurrence (any or invasive), following lumpectomy with negative margins but prior to the decision or recommendation for radiation therapy.	Based on a review of data and discussion, the panel consensus did not support the addition of these specific recommendations into the Guidelines. See Submission for references.	0	21	0	7
BINV-6 Internal request from Institutional Review. 1. For node positive patients, adjuvant chemotherapy is still being recommended universally without consideration for gene profiling assays. Aren't MammaPrint or Oncoytpe Dx now recommended particularly when there are only 1-3 positive SLNs? This point is referenced in footnotes gg and hh, but it might be timely to make this more prominent by stating "consider genomic assay for 1-3+ nodes to determine need for chemotherapy". 2. pN1mi for tumors < 0.5 cm, consider adding 21 gene assay for determination of chemotherapy usefulness. 3. N1 disease – consider adding 21 gene assay or mammaprint test for testing for efficacy of chemotherapy. 4. The flow chart needs to be updated to reflect TAILORx. This may need to be discussed at full committee given complicated structure, but something indicating for RS<25 in postmenopausal women no chemo, for > 31 chemo, for 25-31 consider chemo but individualize. For premenopausal women, for 15-25 there may be some benefit and need to individualize. 5. Consider TAILORx results and move lower limit of chemotherapy + endocrine therapy to RS=25. 6. Add footnote to indicate that for women <50 with intermediate rRS, the lower limit for considering chemotherapy should be around 15. 7. While awaiting results of RxPONDER, consider endocrine therapy alone for patients with 1-3+LN and RS	The Panel reviewed the available data and the submissions related to use of multigene assays to determine the benefit of adjuvant chemotherapy in patients with hormone-receptor positive, HER2-negative early stage breast cancer and has provided recommendations for considerations of multigene assays for addition of adjuvant chemotherapy to adjuvant endocrine therapy in these patients based on nodal status. The panel also developed a table for reference listing the available multigene assays along with details regarding their predictive/prognostic value, NCCN categories, and treatment implications (See page BINV-M of the NCCN Guidelines for Breast Cancer). See Submissions for references.	21	0	0	7

<11 (or even <18), based on the SEER, CLALIR and German databases. 8. Can the panel please consider modifying the algorithm to reflect the data from the TAILORx trial (i.e. changing cutpoints, mentioning impact of age on decisions re chemo?) 9. Given that availability of data supporting the use of assays besides Oncotype Dx for decisions regarding chemotherapy (ie. Mammaprint, 2016 NEJM publication), some providers at our institution request that the panel reconsider incorporation of other assays into the guidelines as was done in the ASCO guidelines (Harris L 2016 JCO). Perhaps additional assays could be listed as options to "consider" as opposed to "recommended" while Oncotype remains "recommended"? 10. Adjust guidelines to reflect TAILORx data for women < and > 50 yo. 11. Update the Guidelines to include TAILORx findings.					
<u>BINV-6</u> <u>External request from Agendia Inc.</u> 1. BINV-6: Move N1mic to Node+ branch, 1-3 LN+, and classify tumors by pT size and LN status. 2. For LN – tumors >0.5cm, replace "consider 21-gene RT-PCR assay" with "recommend 70-gene MammaPrint gene expression assay" with retention of the "ff" footnote. The algorithm may then split into two branches: 70 gene Low Risk – adjuvant endocrine therapy alone and 70 gene High Risk – adjuvant chemotherapy + endocrine therapy. 3. The language in the "ff" footnote should be amended to "Other multigene assays may be considered to help assess risk of recurrence but have not been validated with prospective randomized evidence to predict the lack of clinically meaningful benefit of chemotherapy" 4. For LN +, 1-3 nodes, add "recommend 70-gene MammaPrint gene expression assay" with addition of the "ff" footnote. The algorithm may then split into two branches: 70 gene Low Risk – adjuvant endocrine		21 0 0	0 21 21	0 0 0	7 7 7

therapy alone and 70 gene High Risk – adjuvant chemotherapy + endocrine therapy.		0	21	0	7
BINV-6 External request from Genomic Health. Remove the word **"consider"** from the pN0 and pN1mi (micrometastatic) component of the invasive breast cancer algorithm.		21	0	0	7
BINV-6 External request from Genomic Health. Add a notation of (category 1), and indicate in a footnote "for those eligible for chemotherapy". Change the specific treatment recommendations based on the Recurrence Score result to the TAILORx-defined cutpoints for chemotherapy benefit.		21	0	0	7
BINV-6 External request from Genomic Health. Elevate the 21-gene RT-PCR assay from "footnote gg" on page BINV-6 to the clinical algorithm as a component of the initial work-up for patients after diagnosis with early stage ER+, HER2- invasive breast cancer with 1-3 positive lymph nodes, and add the word "consider" in a manner consistent with use of the 21-gene RT-PCR assay for node-negative patients as described in the 2017 guidelines		21	0	0	7
BINV-6 External request from NanoString. 1. Request to modify the decision tree/treatment algorithm by referring to genomic signatures as a class rather than specifically naming only the 21-gene assay, including removal of specific score ranges in favor of Low, Intermediate, and High-Risk group terminology or expression of the risk of distant recurrence at 10 years as percentage probabilities (Low = <10%, Intermediate = 10%-20%, High = >20%). 2. Request to modify the footnote 'gg' to include the 50-gene assay (PAM50) as an option for lymph node-positive (1-3 positive nodes) disease.		21	0	0	7

BINV-6 External request from Myriad. Change footnote gg to: The 12-gene recurrence test (EndoPredict from Myriad Genetics) can be used to identify node positive patients with very low 10-year risk of recurrence for whom chemotherapy may be unnecessary.		21	0	0	7
BINV-10 External request from Genomic Health. 1. Request the NCCN Breast Cancer Panel to add the use of the 21-gene RT-PCR in the preoperative work-up in women with ER-positive, HER2-negative breast cancer during the work-up of the patient.	Based on a review of data and discussion, the panel consensus did not support the addition of these specific recommendations into the Guidelines. See Submission for references.	0	21	0	7
BINV 17, BINV-21, BINV-23: External request from Foundation Medicine, Inc. Include comprehensive genomic profiling (CGP), via a single assay (as opposed to sequential testing of single biomarkers), in the initial evaluation of a patient with recurrent or Stage IV breast cancer to identify genomic alterations in *PIK3CA, ERBB2* (HER2), *ESR1, BRCA1/2, AKT1*, and genes regulating the cell cycle, as well as other driver alterations that may inform the patient's treatment, including the option to enroll in genomically matched clinical trials.	Based on a review of data and discussion, the panel consensus did not support the addition of these specific recommendations into the Guidelines. See Submission for references.	0	21	0	7
BINV-A External request from Foundation Medicine, Inc. Request CGP be included in the "Principles of HER2 testing" as a method to identify *ERBB2* short variant mutations that are not assessed by routine HER2 testing methods.	Based on a review of data and discussion, the panel consensus did not support the addition of these specific recommendations into the Guidelines. See Submission for references.	0	21	0	7
BINV-L External request from Genomic Health. Add language in as follows: Preoperative endocrine therapy alone may be considered for patients with ER-positive, HER2-negative breast cancer with a 21-gene RT-PCR assay result that has been shown to predict for a lack of chemotherapy benefit when given in the adjuvant setting.	Based on a review of data and discussion, the panel consensus did not support the addition of these specific recommendations into the Guidelines. See Submission for references.	0	21	0	7