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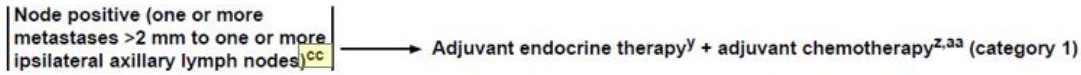
| NCCN Guidelines Panel: | August 4th, 2017 |


Specific Changes: On page BINV-6:




[b] See Principles of HER2 Testing (BINV-A).
[w] Mixed lobular and ductal carcinoma as well as metaplastic carcinoma should be graded based on the ductal component and treated based on this grading. The metaplastic or mixed component does not alter prognosis.
[y] Evidence supports that the magnitude of benefit from surgical or radiation ovarian ablation in premenopausal women with hormone receptor-positive breast cancer is similar to that achieved with CMF alone. See Adjuvant Endocrine Therapy (BINV-J) and Preoperative/Adjuvant Therapy Regimens (BINV-K).
[z] Chemotherapy and endocrine therapy used as adjuvant therapy should be given sequentially with endocrine therapy following chemotherapy. Available data suggest that sequential or concurrent endocrine therapy with radiation therapy is acceptable. See Adjuvant Endocrine Therapy (BINV-J) and Preoperative/AdjuvantTherapy Regimens (BINV-K).
[aa] There are limited data to make chemotherapy recommendations for those >70 y of age. See NCCN Clinical Practice Guidelines for Older Adult Oncology.
[cc] The 21-gene RT-PCR assay recurrence score can be considered in select patients with 1–3 involved ipsilateral axillary lymph nodes to guide the addition of combination chemotherapy to standard hormone therapy. A retrospective analysis of a prospective randomized trial suggests that the test is predictive in this group similar to its performance in node-negative disease.
[dd] Other prognostic multigene assays may be considered to help assess risk of recurrence but have not been validated to predict response to chemotherapy.

Change footnote cc 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.

Rationale: The footnote presently endorses use of 21-gene RT-PCR assay (Oncotype Dx from Genomic Health) for risk assessment in this patient population; however, low risk patients identified with this assay have a 25-40% risk of recurrence[1,2] and the test is only prognostic over 5 years. Endopredict's EPclin score identifies node positive patients with very low risk of recurrence (5% over 10years[1]), the rate for EPclin low risk patients with node positive disease is thus lower than that for node *negative* RS-low patients (5.3%), for whom the panel currently recommends endocrine therapy only. These new data support rewording the footnote so that oncologists are aware of the opportunity to identify node positive patients with exceedingly low 10-year risk of recurrence and who may wish to consider forgoing chemotherapy.

References


1.Buus R, Sestak I, Kronenwett R, et al. Comparison of Endopredict and EPclin with Oncotype DX score for prediction of risk of distant recurrence after endocrine therapy [supplemental materials]. *J Natl Cancer Inst.* **2016** 108(11): djw149

2. Albain KS, Barlow WE, Shak S, et al. Prognostic and predictive value of the 21-gene recurrence score assay in postmenopausal women with node-positive, oestrogen-receptor-

positive breast cancer on chemotherapy: a retrospective analysis of a randomised trial. *Lancet Oncol.* **2010** 11(1):55-65

3.Filipits M, Rudas M, Jakesz R, et al. A new molecular predictor of distant recurrence in ER-positive, HER2-negative breast cancer adds independent information to conventional clinical risk factors. *Clin Cancer Res*. **2011** 17(18):6012-6020.

Sincerely,

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