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 NCCN Guidelines Panel: Breast Cancer

Specific Changes: On page BINV-6:

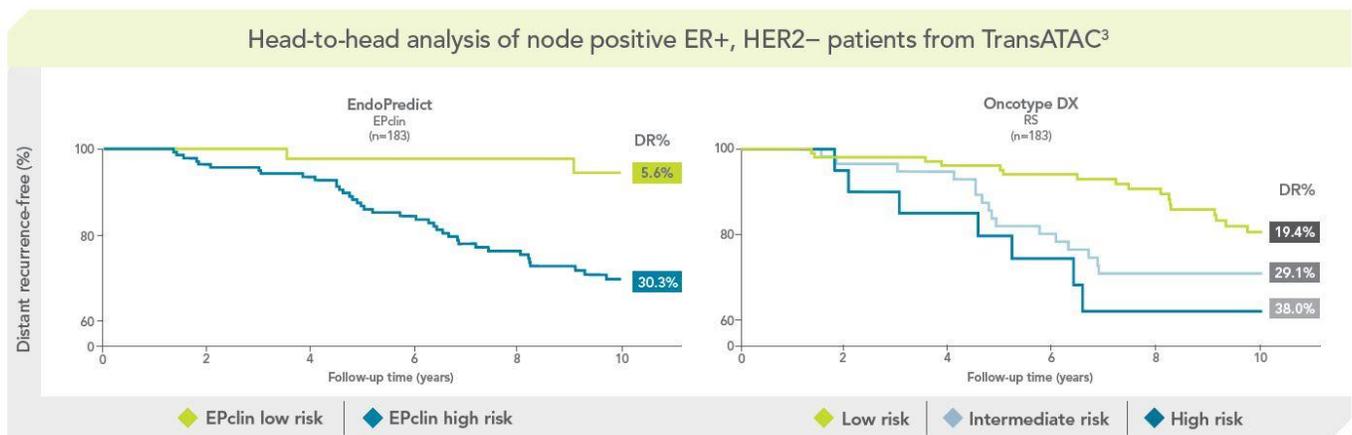
Node positive (one or more metastases >2 mm to one or more ipsilateral axillary lymph nodes)^{gg} → **Adjuvant endocrine therapy^{z,aa} + adjuvant chemotherapy^{bb,cc} (category 1)**

^{gg}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.

^{hh}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 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.

Rationale: The footnote presently endorses use of the 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 19-40% risk of recurrence^{1,2,4}. EndoPredict’s EPclin score identifies node positive patients that are truly low risk, shown to have a 10-year risk of recurrence of 5.0%^{1,2}. The rate for EPclin low risk patients with node positive disease is thus lower than that for node *negative* RS-low patients (5.9%)⁴, 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 have good outcomes with endocrine therapy only.



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.
4. Sestak I, Buus R, Cuzick J, et al. Comparison of the performance of 6 prognostic signatures for estrogen receptor-positive breast cancer. *JAMA Oncology* **2018**;4(4):545-553.

Sincerely,

A handwritten signature in black ink, appearing to read 'Johnathan Lancaster', written in a cursive style.

Johnathan Lancaster, MD, PhD
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Myriad Genetic Laboratories Inc.