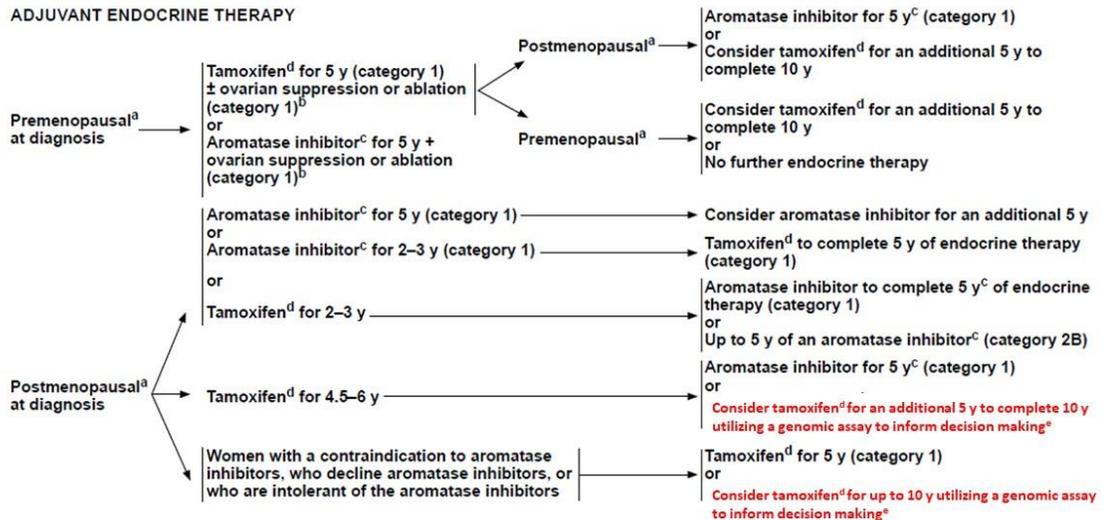


Submitted by: Chief Medical Officer
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 Date of request: July 23, 2019
 NCCN Guidelines Panel: Breast Cancer (Treatment)

Specific Changes: To add guideline verbiage in support of the utilization of genomic assays to inform extended endocrine therapy decisions.

1. On page BINV-17, amend the first bullet point under Endocrine Therapy to read: **“Assess and encourage adherence to adjuvant endocrine therapy informed by results of genomic assay”^{yy}**
 - a. **ADD footnote “yy”: Late recurrence (5-15yrs) data (Filipits, et al., 2019) indicates that patients may consider foregoing extended endocrine therapy with EndoPredict low risk (EPclin ≤3.3) scores.**
2. On page BINV-K, amend postmenopausal at diagnosis branch of the algorithm to include language in support of the utilization of genomic assays to guide extended endocrine therapy. See recommended changes in graphic below:
 - a. **ADD footnote “e”: Late recurrence (5-15yrs) data (Filipits, et al., 2019) indicates that patients may consider foregoing extended endocrine therapy with EndoPredict low risk (EPclin ≤3.3) scores.**



FDA Clearance: Not applicable.

Rationale: We requested consideration for the recommendation of all [newly diagnosed] ER+, HER2-, N0 and N1 (1-3 nodes) early stage breast cancer patients be tested with a genomic assay [breast prognostic] with long-term outcome data (5-15yrs) to aid in guiding adjuvant endocrine therapy 5 years post diagnosis.

Filipits, et al. 2019 conducted a re-analysis of the randomized phase III ABCSG-6/8 clinical trial cohorts to a maximum of 16.6 yrs (median 9.6 yrs which is 4.3 yrs longer than previous analysis). 1,386 women were distant recurrence free at 5 years post diagnosis and were assessed for late distant recurrence. The 5-15 year late distant recurrence in these women was 4.3% (6.6%, 1.9%) in low EPclin risk scores (≤ 3.3) versus 15.9% (21.1%, 10.4%) in EPclin high risk scores (> 3.3) (HR 4.52 [2.65, 7.72], $p > 0.0001$). This data demonstrates the prognostic power of EPclin in predicting late distant recurrence which may aid in identifying patients that can safely forego endocrine therapy at five years.

Reference:

Filipits, et al.: Prediction of Distant Recurrence using EndoPredict among Women with ER+, HER2- Node-Positive and Node-Negative Breast Cancer Treated with Endocrine Therapy Only. Clin Cancer Res 25:1-8, 2019.

Sincerely,

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

Johnathan Lancaster, MD, PhD
Chief Medical Officer, Myriad Genetic Laboratories Inc.