NCCN Guidelines Panel: Breast Cancer

On behalf of Genomic Health, Inc., I respectfully request that the NCCN Breast Cancer Panel review the enclosed publications 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.

**Specific Changes:** Include the 12-gene DCIS Score™ assay as a component of the initial work-up for patients diagnosed with DCIS, following lumpectomy with negative margins (page DCIS-1)

**FDA Clearance:** FDA clearance is not required for this assay because it is performed in the central laboratory at Genomic Health, which is regulated and certified under the Clinical Laboratory Improvement Amendments (CLIA) and the College of American Pathologists (CAP).

**Rationale:** In support of the proposed change, the 12-gene DCIS Score assay was validated in two prospectively designed studies to predict 10-year risk of any or invasive local recurrence in patients with DCIS after breast-conserving surgery alone (BCS)\(^1,2\) or after BCS plus radiation therapy.\(^3\) DCIS Score results added information beyond what was discerned by clinicopathologic factors alone.\(^1,3\) Estimates of 10-year risk of local recurrence were further refined in a meta-analysis that combined both BCS-alone studies, showing that 47% of patients can be identified with a ≤10% risk of local recurrence over 10 years.\(^4\) Subsequent to that publication, further prediction modeling was done including 1102 cases of DCIS comparing clinicopathologic features (CPF) versus CPF + ER and HER2, versus CPF + 12-gene DCIS score (DS). Individual prediction of locoregional recurrence (LR) incorporating CPF and DS was more accurate and identified a higher proportion of women with a low predicted risk of LR after BCS alone, for whom radiotherapy may be omitted.\(^5\)

Shared decision-making in healthcare is realized when both patient and physician contribute to care decisions based on available information. In this capacity, the individualized risk estimates provided by DCIS Score results can support shared decision-making, such that patients can avoid radiation-related morbidity when their risk of recurrence is low or feel confident in their decision to have radiation therapy when their risk of recurrence is high. In support of the clinical utility of the DCIS Score assay, physicians in two prospective, multicenter decision impact studies changed recommendations for radiation therapy for about 30% of their patients, based on DCIS Score results.\(^6,7\) In addition, a recent publication of ECOG E1142 trial showed that for women who underwent BCS for DCIS, 93% were adherent to the recommendation either supporting or discouraging the use of radiation therapy based on the 12-gene DCIS score result.\(^8\)

The following articles are submitted in support of this proposed change.

Sincerely,

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