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July 3, 2018

NCCN Guidelines Panel: Breast Cancer

On behalf of Genomic Health, Inc., I respectfully request, based on the publications listed below, that the **NCCN Breast Cancer Panel** update the NCCN guidelines for the **Oncotype DX Breast Recurrence Score<sup>®</sup>** (RS) assay, also known as the 21-gene RT-PCR assay, in the initial work-up for patients diagnosed with early stage ER+, HER2-negative, lymph node-positive (1-3 nodes) breast cancer, to stratify patients by risk of recurrence and identify patients with likely chemotherapy benefit.

Specific Changes: 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 (BINV-6).

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 these changes, the 21-gene RT-PCR assay was validated in node-positive patients in two prospectively designed studies to predict risk of distant recurrence and identify patients who are likely to benefit from chemotherapy.<sup>1,2</sup> More recently, prospective outcomes in >7K node-positive patients (1-3 positive nodes) have been reported in three studies, including the prospective phase III WSG PlanB study showing 5-year disease free survival data in patients treated with endocrine therapy alone,<sup>3</sup> the SEER registry showing 5-year breast cancer specific mortality data,<sup>4,5</sup> and the Israeli Clalit registry showing 5-year distant recurrence data.<sup>6</sup> All of these studies show that patients with limited node involvement and low RS results have highly favorable outcomes when treated with endocrine therapy alone, providing strong and consistent support that the 21-gene RT-PCR assay provides important prognostic information in node-positive disease that is invaluable when deciding upon optimal systemic therapy.

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

1. Dowsett M, Cuzick J, Wale C, et al. Prediction of risk of distant recurrence using the 21-gene recurrence score in node-negative and node-positive postmenopausal patients with breast cancer treated with anastrozole or tamoxifen: a TransATAC study. *J Clin Oncol.* 2010;28(11):1829-1834. [[TransATAC; validation of the 21-gene RT-PCR assay for prognosis](#)]
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. [[SWOG 8814; validation of the 21-gene RT-PCR assay for prediction of chemotherapy benefit](#)]
3. Nitz U, Gluz O, Christgen M, et al. Reducing chemotherapy use in clinically high-risk, genomically low-risk pN0 and pN1 early breast cancer patients: five-year data from the prospective, randomised phase 3 West German Study Group (WSG) PlanB trial. *Breast Cancer Res Treat.* 2017;165(3):573-583. [[PlanB; prospective 5-year outcomes for RS <12](#)]

4. Roberts MC, Miller DP, Shak S, Petkov VI. Breast cancer-specific survival in patients with lymph node-positive hormone receptor-positive invasive breast cancer and Oncotype DX Recurrence Score results in the SEER database. *Breast Cancer Res Treat.* 2017;163(2):303-310. [[SEER/NCI; real-world 5-year outcomes for RS <18](#)]
5. Petkov VI, Miller DP, Howlander N, et al. Breast-cancer-specific mortality in patients treated based on the 21-gene assay: a SEER population-based study. *npj Breast Cancer.* 2016;2:16017. [[SEER/NCI; real-world 5-year outcomes for RS <18](#)]
6. Stemmer SM, Steiner M, Rizel S, et al. Clinical outcomes in ER+ HER2- node-positive breast cancer patients who were treated according to the Recurrence Score results: Evidence from a large prospectively designed registry. *npj Breast Cancer.* 2017;3(1)32. [[Clalit; real-world, prospective 5-year outcomes for RS <18](#)]

Sincerely,

A handwritten signature in black ink that reads "Christy A. Russell, MD". The signature is written in a cursive style with a large initial 'C' and a distinct 'MD' at the end.

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Senior Director, Medical Affairs  
Genomic Health, Inc.