INTRODUCTION

• Breast Cancer Index (BCI) is a validated gene expression-based assay that integrates the molecular grade index (MGI) and the two-gene ratio HOXB13/L17B8 (H1) that evaluate tumor proliferation and estrogen signaling, respectively.
  o Integration of MGI and H1 generates a prognostic BCI score that significantly predicts risk of overall (10y), early (0-5y), and late (≥5y) distant recurrence (DR) in HR+, node-negative (N0) and node-positive (N1) breast cancer.
  • The N1 prognostic model (BCIN+) integrates tumor size and grade.
  • The H1 ratio is the predictive component of BCI and has been shown to predict endocrine response across various treatment regimens.
  • The current prognostic model, BCIN+, was trained in the Trans-ATAC (Arimidex, Tamoxifen, Alone or in Combination) cohort, which randomized patients at the time of diagnosis to either primary adjuvant anastrozole versus tamoxifen.1
  • The IDEAL (Investigation on the Duration of Extended Letrozole) trial randomized patients that completed 5 years of endocrine therapy and compared additional 5 vs 2.5y of extended letrozole providing a cohort that specifically evaluated late DR.
  • The aim of the current study was to specifically evaluate prognostic performance of BCIN+ in a late DR cohort.

METHODS

• Patients with 1 to 3 positive nodes (N1) randomized within 6 years from surgery in the 7.5-year endocrine treatment arm of the translational IDEAL cohort (Figure 1) were used to examine cut-points for the BCIN+ model across a range of 0 to 10 years and categorized patients into Low- and High-risk groups.
  • Kaplan-Meier analysis was used to calculate the 15y (post-diagnosis, 10y post-randomization) late distant recurrence free survival (DRFS) as the primary endpoint.
  • The BCI assay cut-point was selected based on the classification of a Low-risk group with maximum number of patients and with >95% 15y late DRFS.
  • Initial validation of the optimized prognostic model was performed in an institutional retrospective cohort from Massachusetts General Hospital (MGH) using Cox proportional hazards regression.

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Age at surgery</th>
<th>IDEAL N1</th>
<th>MGH N1</th>
<th>P-value</th>
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<tbody>
<tr>
<td>N=277</td>
<td>75.4%</td>
<td>84.8%</td>
<td>&lt;0.001</td>
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RESULTS

• Of the 218 N1 IDEAL patients included, 71% were ≥50y, 55% had T1 tumors, and 51% were grade 2 (Table 1).

Figure 2. Optimized BCIN+ in IDEAL N1 Cohort

- A cut-point of 1.8 was selected to ensure >95% 15y late DRFS for BCIN-Low risk group.
- In the optimization cohort, 20% patients were classified as BCIN+ Low-Risk with 15-year late DRFS 96.8% (HR: 9.45, 95% CI: 1.01-54.71; p=0.020) (Figure 2).

CONCLUSIONS

• A new optimized cut-point of BCIN+ scores was identified for node positive patients using the IDEAL N1 subset.
  • The cut-point was chosen to ensure the 15-year risk of late DR was greater than 95% (96.8% in IDEAL N1).
  • The cut-point was validated in the independent MGH N1 cohort for late DR.
  • Additional studies in randomized extended endocrine trial N1 cohorts are required for further validation of this BCIN+ model optimized for late DR.

REFERENCES