Clinical Validation

In Women With Estrogen Receptor-Positive (ER+), Human Epidermal Growth Factor Receptor 2-Negative (HER2-) Primary Breast Cancer

digistain™

Introduction

The Digistain™ technology uses a well-established analytical technique (infrared multi-spectral imaging) that operates biologically downstream from genomics to avoid recognised challenges that originate from tissue processing variabilities. The technique uses a proprietary spectral signature demonstrated to be **97% reproducible** and enables precise quantification of long-established pathology markers correlated to chromosomal instability (CIN) and tumor proliferation including nuclear pleomorphism and mitotic activity to produce a personalized risk score.

Study Highlights

1. **HIGH ACCURACY AND PREDICTIVE PERFORMANCE**
   In HR-positive HER2-negative primary operable breast cancer and ≤3 positive lymph nodes
2. **CLASSIFIES PATIENTS AS LOW OR HIGH RISK**
   With similar accuracy and predictive performance as that reported for other risk stratification tools
3. **CLINICAL UTILITY**
   For low-cost, rapid and widely accessible prognostic testing

Study Design

- Early stage, ER+, HER2- primary breast tumor samples from women who were systemically treated with adjuvant endocrine therapy alone were obtained from the well characterized and published patient cohort from University Hospital of Nottingham UK.
- Primary Objective: To evaluate the DPS (Digistain Prognostic Score - a continuous variable) and 10-year recurrence-free survival (RFS).

Methods

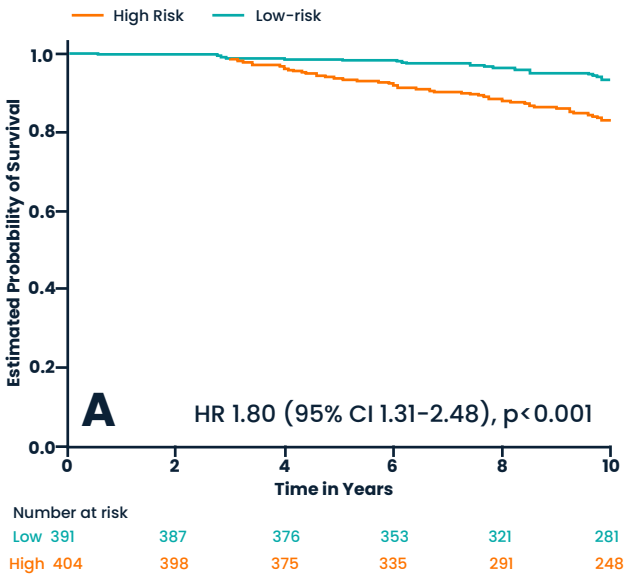
- FFPE patient samples of primary tumor invasive breast cancer tested retrospectively with Digistain in a double blinded setting to produce a DPS (in combination with Digistain Index, histological tumor grade, pathologic tumor size and patient age)
- Association of DPS with 10-year RFS was evaluated using Cox Proportional Hazards models stratified by cohort.
- The DPS model is based on the unbiased supervised analysis with a N x K fold cross validation procedure.
- 10-year RFS was estimated using DPS for high and low risk by Kaplan Maier analysis with the predetermined cut-off for high and low risk classification corresponding to 10% risk.

Detailed Results

- 801 patients were included in the analysis with a median follow-up of 12.7 years.
- Both Digistain Index (HR = 4.41, p<0.05) and DPS (HR = 1.8, p<0.001) were strongly associated with increased risk of recurrence.
- 49% of patients in the cohort were classified as low risk.
- 10-year RFS: DPS high risk group had a significantly increased risk of mortality compared to the low-risk group.
- In multivariate Cox-Proportional Hazard analysis Digistain Index had the most significant hazard ratio.
- Multivariate Cox-Proportional Hazard analysis of Digistain Index and clinico-pathological factors demonstrated that Digistain Index , tumor size, histological tumor grade, patient age and tumor size were all significantly associated with disease free survival.

Conclusion

- In this study, with a median follow-up time of 12.7 years, the DPS was highly associated with RFS in ER+, HER2- early-stage primary tumor breast cancer patients who received adjuvant endocrine therapy alone.
- Based on these data, women with DPS low risk breast cancer with up to 3 lymph nodes may safely forgo adjuvant chemotherapy in favour of endocrine therapy.



Graph demonstrates Digistain ability to characterise previously unidentified low risk patients suitable for the safe avoidance of adjuvant chemotherapy.

Bottom Line

1. Digistain has been validated in early-stage ER+, HER2- breast cancer patients.
2. These data highlight the importance of testing patients with Digistain prior to adjuvant chemotherapy decisions.
3. Digistain identified 49% patients with low-risk disease (using a robust cross-validation model) who may safely forgo adjuvant chemotherapy.

References

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