DCISionRT®

The American Society for Radiation Oncology 2022

Title: Re-thinking Clinicopathologic Risk Assessment in DCIS: Pooled Data from Validation Studies Comparing a 7-gene DCIS Assay to Clinicopathologic Features Alone

Background: There is a need for a tool to predict recurrence risk and RT benefit to enable personalized management of DCIS after breast conserving surgery (BCS). Clinicopathologic (CP) factors alone have failed to identify a low-risk group with little benefit from RT, or a high-risk group with high recurrence risk after RT. The purpose of this study was to prospectively validate a novel biosignature, Residual Risk Subtype (RRt), integrated with the 7-gene DCIS assay to assess 10yr ipsilateral breast recurrence (IBR) rate and RT benefit compared to CP criteria alone.

Methods: Women (n=926) from four international cohorts treated with BCS with negative margins had FFPE tissue samples analyzed at a CLIA lab (Laguna Hills CA). The 7-gene DCIS biosignature combines biomarkers with CP factors (age, size, palpability, and margin status) using an algorithm and reports a decision score (DS). Women were classified into 3 risk groups by the biosignature DS (0-10) integrated with RRt (yes/no): 1) Low Risk(DS≤2.8 without RRt), 2) Elevated Risk (DS>2.8 without RRt), 3) Residual Risk (DS>2.8 with RRt). Within the 3 biosignature risk groups, 10yr IBR Kaplan-Meier rates by RT treatment and Cox proportional hazard ratios for RT-effect were assessed and reported by CP criteria (nuclear grade, palpability, screening detection, size, and age), including RTOG 9804 study 'good-risk' groupings.

Results: The biosignature classified 37% of the women as Low Risk with low 10yr IBR rates with or without RT and 43% as Elevated Risk with a 20.6% IBR rate without RT and an 80% IBR benefit from RT (4.9%), which persisted even in good risk CP patients (see table). 20% of women were classified as Residual Risk and had a 42.1% IBR rate without RT and a significantly elevated IBR rate of 14.7% after RT. The distribution of patients in the 3 biosignature risk groups differed between CP criteria (RTOG 9804 'good-risk', or young age or high grade). However, once classified into these 3 biosignature risk groups, the 10yr IBR rates and RT benefit were independent of CP criteria. About 30% of women with a high-risk CP profile were re-classified as Low Risk with almost no benefit of RT while ~30% were re-classified as Residual Risk. In women with favorable CP criteria, more than 50% were reclassified as Elevated Risk or Residual Risk patients with significant IBR risk remaining after BCS.

Conclusions: The predictive 7-gene DCIS assay integrated with the novel Residual Risk Subtype (RRt) biosignature classified women into 3 risk groups with distinct 10yr IBR rates and RT-benefit profiles. Within biosignature risk groups, CP criteria were not prognostic or predictive for 10yr IBR rates or RT benefit while a clear delineation was seen for the 3 biosignature risk groups. The incorporation of genomic information yields superior risk and RT benefit prediction as compared to CP features alone.

Authors:

Chirag Shah,
Cleveland Clinic Taussig Cancer Institute, Cleveland, OH

Frank Vicini, MD
GenesisCare, Farmington Hills, MI

Fredrik Wärnberg, MD PhD
University of Gothenburg, Gothenburg, Sweden

Sheila Weinmann, MPH PhD
Kaiser Permanente Center for Health Research, Portland, OR

G Bruce Mann, MBBS PhD
Royal Women's Hospital, Parkville, Australia

Rachel A. Rabinovitch, MD
University of Colorado Cancer Center, Aurora, CO

Pat Whitworth, MD
Nashville Breast Center, Nashville, TN

Julie A. Margenthaler, MD
Washington University School of Medicine, St Louis, MO

Michael Leo, PhD
Kaiser Permanente Center for Health Research, Portland, OR

David J. Dabbs, MD
PreludeDx, Laguna Hills, CA

Karuna Mittal, PhD
PreludeDx, Laguna Hills, CA

Steven C. Shivers, PhD
PreludeDx, Laguna Hills, CA

Troy Bremer, PhD
PreludeDx, Laguna Hills, CA