DCISionRT®

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**Title:** Assessing the benefit of adjuvant endocrine therapy in patients following breast-conserving surgery with or without radiation stratified by a 7-gene predictive DCIS biosignature.

**Background:** Breast conserving surgery (BCS) followed by radiotherapy (RT) has been the mainstay for DCIS treatment. Adjuvant endocrine therapy (ET) has often been recommended based on multiple randomized clinical trials (RCT). However, these studies have failed to identify subsets of patients who did or did not benefit from adjuvant RT/ET therapy after BCS. We evaluated the association of a 7-gene predictive DCIS biosignature (PreludeDx, Laguna Hills, CA) to assess the impact of ET on 10-yr ipsilateral breast recurrence (IBR) risk after BCS alone or with RT.

**Methods:** DCISionRT with integrated Residual Risk subtype (RRt) reported a decision score (DS) and three risk groups, a) Low Risk (DS≤2.8), b) Elevated Risk (DS > 2.8 without RRt) and c) Residual Risk (DS > 2.8 with RRt). DCISionRT/RRt was evaluated in 926 patients from 4 cohorts who were treated with BCS alone or with RT/ET. The three risk groups were assessed for 10-yr total (invasive and in situ) IBR risk by Kaplan Meier and Cox proportional hazards survival analysis.

**Results:** DCISionRT/RRt classified 338 (37%) women as Low Risk, 399 (43%) as Elevated Risk, and 189 (20%) as Residual Risk. Overall, patients treated with ET had a significantly lower 10-yr IBR risk in multivariable analysis independent of RT (HR = 0.55, p = 0.033). In the Low Risk group treated with BCS without RT, the average 10-yr IBR risk was 5.6% (95% CI 2.5-12.1%, n = 124) and was not significantly different with vs without ET (p = 0.33). The 10-yr IBR risk after BCS alone was 22.6% in the Elevated Risk group and 50.3% in the Residual Risk group. Compared to BCS alone, the 10-year IBR risk tended to be lower in patients prescribed ET without RT in the Elevated (11.6%, 95% CI 3.9-32%) and Residual (15.4%, 95% CI 4.1-49%) Risk groups. 10-yr IBR risk was not significantly reduced by RT within the Low Risk group (p = 0.7) but was significantly reduced to 6.3% (95% CI 3.4-12%) by RT within the Elevated Risk (HR = 0.2, p < 0.001) and to 12.5% (95% CI 6.4-23%) within the Residual Risk (HR = 0.2, p < 0.001) groups. 10-yr IBR risk was significantly higher after RT in the Residual (HR = 2.5, p = 0.013) vs. Elevated Risk groups. After BCS and RT, there was no significant reduction in 10-yr IBR risk for those treated with vs without ET in the Elevated (p = 0.22) and Residual (p = 0.87) risk groups.

**Conclusion:** The DCISionRT/RRt biosignature demonstrated prognostic and predictive RT response in Elevated and Residual Risk patients. Consistent with prior RCT data, ET was associated with lower 10-yr IBR risk overall, and within the DCISionRT Elevated and Residual Risk groups without RT. However, neither ET nor RT were asssociated with significant risk reduction in the Low Risk group. There was no added benefit of ET in the Elevated and Residual Risk groups after BCS+RT; the Residual Risk group patients still had a high IBR risk after RT.

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