The Impact of DCISionRT Versus Clinicopathologic Factors Alone in Predicting Benefit of Radiation

By Amishi Bajaj, MD – February 28, 2024

For clinicians treating breast cancer, a favorite question of patients and their loved ones is, "Do you have a test to predict the need for radiation like the one the chemotherapy doctors use?"

With the implementation of the DCISionRT *(PreludeDx, Laguna Hills, CA)* 7-gene biosignature into clinical practice, radiation oncologists are now able to provide patients with DCIS more personalized treatment recommendations regarding pursuing adjuvant radiation treatment or omitting, as the DCISionRT clinicogenomic biosignature is both prognostic for recurrence risk after breast-conserving surgery as well as predictive for benefit of radiation treatment. [1] This is in contrast to the Oncotype DX DCIS *(Exact Sciences, Madison, WI)* score, which also predicts local recurrence risk but does not allow for predicting the extent of individualized benefit for patients receiving adjuvant radiation. When DCISionRT is not utilized, the clinical decision-making surrounding administration of adjuvant radiotherapy comes down to clinician judgment and assessment of risk factors for recurrence risk, such as patient age, tumor size, clinical detectability, and margin status – underscored risk features following publication of data from studies investigating adjuvant radiation versus observation for patients with DCIS status post breast-conserving surgery.

The Research Question

Following the implementation of a clinical tool comes the need to investigate its usefulness: To what extent does the DCISionRT biosignature predict for local recurrence events as compared to only clinicopathologic factors? Even using clinicopathologic factors, prospective trials have not been able to elucidate a patient group that did not benefit from radiation, but what about when DCISionRT is utilized? At the 2023 ASTRO Annual Meeting, these questions are answered. Investigators sought to determine if patients who were historically considered "low risk" by clinicopathologic factors could be re-stratified into risk groups as determined by the DCISionRT 7-gene biosignature and if this re-stratification would be associated with 10-year ipsilateral breast recurrence events.

Methodology & Results

Using four international cohorts of patients with DCIS status post breast-conserving surgery (n=926), formalin-fixed paraffin embedded tissue samples were analyzed (CLIA lab, Laguna Hills, CA) to ascertain the DCISionRT biosignature for all patients. In terms of assessment of clinicopathologic factors, criteria from RTOG 9804 (nuclear grade 1-2, size ≤2.5 cm, screening-detected/non-palpable tumor, negative surgical margin) were employed along with criteria supported by the *Memorial Sloan Kettering Cancer Center* (MSKCC) DCIS nomogram (age at diagnosis, family history, clinical presentation, presence of necrosis, receipt of adjuvant endocrine therapy, etc) based on a calculator score while excluding patients with close margins and any re-excisions. Combining the DCISionRT biosignature reported a Decision Score and a Residual Risk subtype (with residual risk implying worse outcomes than otherwise expected even with adjuvant radiotherapy), and using these, patients with low-risk clinicopathologic

factors were then categorized as DCISionRT Low Risk (no residual risk subtype, Decision Score ≤2.8) or DCISionRT High Risk (any Residual Risk plus Decision Score >2.8). Ultimately, the study authors determined that the biosignature Low Risk group (n=338) had a 10-year ipsilateral breast recurrence event rate of 5.6% with an absolute radiation benefit of 0.8% – neither statistically nor clinically significant. However, the DCISionRT biosignature found that a number of patients stratified as low risk by clinicopathologic factors were biosignature High Risk, and these patients had higher ipsilateral breast recurrence events for which adjuvant radiation provided an 8-13% absolute reduction in rate of recurrence – both statistically and clinically significant.

What We've Learned

The DCISionRT 7-gene biosignature more reliably predicted higher rates of recurrence for patients who were deemed low risk by clinicopathologic factors but High Risk by biosignature. These patients went on to experience a significant benefit following administration of adjuvant radiation. Accordingly, the DCISionRT 7-gene biosignature also predicted for low-risk patients who would not benefit from adjuvant radiation therapy more consistently than the clinicopathologic factors utilized by RTOG 9804 or the MSKCC nomogram. These new data demonstrate that the DCISionRT biosignature reclassified nearly half of the CP low-risk patients as biosignature high risk with an increased 10-year IBR rate and significant RT benefit.

"Prior to DCISionRT, we relied primarily on traditional clinicopathologic factors to make treatment decisions. We now recognize that those methods are not always accurate at classifying DCIS patients into Low or High-Risk groups and may result in the misclassification of nearly 50% of patients," noted Frank A. Vicini, MD, Radiation Oncologist at Michigan Healthcare Professionals, member of NRG Oncology, and first author of the study.

"DCISionRT is a powerful tool that assists physicians to help identify which patients may have a significant or minimal benefit from radiation therapy based on the patient's individual tumor biology, thus optimizing cross-specialty collaboration, particularly with surgeons, and eliminating unnecessary over- or under-treatment for DCIS patients."

Dr. Vicini went on to say, "Looking into the future, we must advance our tailored treatment decisions with proven, new technologies that enhance patient outcomes. DCISionRT, which also incorporates clinicopathologic factors (CP) into its algorithm, gives us an optimal combination of the past (CP criteria) combined with modern-day tumor biology via molecular testing, resulting in a more reliable method in assisting clinicians to ensure that they are not over- or under-treating patients with low-risk CP."

Well said, Dr. Vicini! I am excited for the future ahead for tailoring treatment to individual patients and providing more personalized care.

Resource

Breast Cancer Nomogram: Ductal Carcinoma In Situ (DCIS) Recurrence [link]

Reference

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