Title: The PREDICT Registry Australia: A prospective registry study to evaluate the clinical utility of the DCISionRT test on treatment decisions in patients with DCIS following breast conserving surgery

Background: The benefit of adjuvant radiation therapy (RT) for women with ductal carcinoma in situ (DCIS) treated with breast conserving surgery (BCS) remains controversial. Since there is level-I evidence supporting the role of RT in reducing the risk of local recurrence, current guidelines generally recommend adjuvant RT for all women having BCS. However, the absolute benefit of RT is variable in women with DCIS and so it is important to develop prognostic and predictive tools to better assess risk and RT benefit. The DCISionRT Test (PreludeDx, LagunaHills, CA) is a biologic signature that provides a validated score (DS) for assessing 10-year risk of recurrence and RT benefit using individual tumor biology, as assessed by clinical and pathologic biomarkers. The primary objective of the PREDICT registries is to understand the decision impact such a tool would have on treatment decisions.

Prospective Clinical Trial Design: This is a multicenter, prospective, non-interventional (observational) cohort study for women diagnosed with DCIS of the breast. After diagnosis of DCIS, sites will send the most representative tissue block or sections mounted on charged slides to PreludeDx for DCISionRT testing. Treating physicians complete a treatment recommendation survey before and after receiving DCISionRT test results. Test results, treatment recommendations, patient preferences and clinicopathologic features will be stored in a de-identified registry for participating institutions from a variety of geographic regions across Australia. Women will then be followed for up to 10 years with completion of a follow-up form. The study has been approved by the North Shore Local Health District Human Research Ethics Committee, St Leonards, NSW, Australia.

Eligibility Criteria: The study includes females age 26 or older who are candidates for BCS and eligible for RT and/or systemic treatment. Subjects must not have been previously treated for DCIS or have previous or current invasive or micro-invasive breast cancer.

Specific Aims: The primary endpoints are changes in treatment recommendations for surgical, radiation and hormonal therapy. Secondary endpoints are identification of key drivers for treatment recommendations, including age, size, grade, necrosis, hormone receptor status and patient preference.

Statistical Methods: Changes in pre- and post-DCISionRT treatment recommendations will be analyzed using McNemar’s test (alpha level = 0.05). Multivariate logistic regression will be used to determine odds ratios of clinicopathologic factors leading to pre- and post-test treatment recommendations. Pre-test covariates include patient age, tumor size, palpability, margin status, hormone receptor status, nuclear grade, tumor necrosis, family history of breast cancer, race, ethnicity and patient preference, as well as physician specialty (surgeons vs. radiation oncologists) and post-test covariates will also include the DCISionRT Decision Score (DS). Differences in recurrence-free and overall survival will be assessed by Kaplan-Meier survival analysis using the log-rank test and/or the Cox Proportional Hazards model. Statistical analyses will be carried out using R (https://www.r-project.org) or SAS. An early interim analysis based on the first 200 enrolled patients is planned.

Present and Planned Accrual: We are planning to enroll up to 1,500 women from up to 100 sites across Australia. A similar registry in the US has enrolled 1,985 women from 64 sites towards a goal of 2,500.
The PREDICT Registry Australia: A prospective registry study to evaluate the clinical utility of the DCISionRT test on treatment decisions in patients with DCIS following breast conserving surgery

Yvonne Zissiadis1, G Bruce Mann2, Steven C Shivers3, Troy Bremer3

1GenesisCare, Perth, WA, Australia; 2Royal Women’s Hospital, Parkville, Vic, Australia; 3PreludeDx, Laguna Hills, CA

Study Design

• The AUS-PREDICT Study has consented 106 women.
• There are 41 sites currently enrolling and additional sites are pending activation.
• The goal is to activate up to 100 sites and consent 1,500 patients diagnosed with DCIS.

Study Groups

• The purpose of the study is to evaluate the percent of cases in which treatment recommendations are changed after the test results become available.

Inclusion criteria:

• Clinical decision has been made to order the DCISionRT test.
• Tissue is available and sufficient for testing.

Exclusion criteria:

• Previous receipt of radiation or systemic treatment.
• Evidence of distant metastases.
• Evidence of an inoperable malignancy.
• Evidence of an invasive malignancy.

Study Population:

The study population will be selected from the clinical practices of the participating investigators and institutions. Patients who have been recently diagnosed with DCIS and are being evaluated for the need for further therapy will be screened for eligibility per the eligibility criteria.

Eligibility Criteria

• Clinical decision has been made to order the DCISionRT test as part of standard care.
• Patient must have histologically confirmed ductal carcinoma in situ (DCIS) in a single breast (presence of lobular carcinoma in situ (LCIS) or other benign breast disease in addition to DCIS is acceptable).
• Patient must be consented within 120 days after surgery.
• Patient must be able to provide informed consent.

Secondary Outcome Measures:

• Distinctly different and complementary to the primary outcome measure.

Other Pre-specified Outcomes:

• Additional secondary outcome measure.

Recruitment

• The study will collect details on physician treatment recommendations before and after availability of the genomic test (DCISionRT) results. The data elements include type of surgery (lumpectomy, thermal ablation, or combination), radiotherapy, and endocrine therapy (yes, no).

Screening Failure

• There are 41 sites currently enrolling and additional sites are pending activation.

Withdrawn

• The goal is to activate up to 100 sites and consent 1,500 patients diagnosed with DCIS.

On Study

• The purpose of the study is to evaluate the percent of cases in which treatment recommendations are changed after the test results become available.

Total Consented

• The AUS-PREDICT Study has consented 106 women.

Current Sites Registered

• There are 41 sites currently enrolling and additional sites are pending activation.

All Sites

• The purpose of the study is to evaluate the percent of cases in which treatment recommendations are changed after the test results become available.

Physician Participation

• The AUS-PREDICT Study has consented 106 women.
• There are 41 sites currently enrolling and additional sites are pending activation.
• The goal is to activate up to 100 sites and consent 1,500 patients diagnosed with DCIS.
• The purpose of the study is to evaluate the percent of cases in which treatment recommendations are changed after the test results become available.

All Investigators

• The AUS-PREDICT Study has consented 106 women.
• There are 41 sites currently enrolling and additional sites are pending activation.
• The goal is to activate up to 100 sites and consent 1,500 patients diagnosed with DCIS.
• The purpose of the study is to evaluate the percent of cases in which treatment recommendations are changed after the test results become available.