DCISionRT®

San Antonio Breast Cancer Symposium 2021

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 insitu (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 ofrecurrence 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.

Universal Trial Number (UTN):
U1111-1266-0439;

ANZCTR:
ACTRN12621000695808;

ClinicalTrials.gov:
NCT04916808.

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.

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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

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Protocol Synopsis	
NCT Number	NCT04916808
Brief Title	The AUS-PREDICT Registry for DCIS Patients With DCISionRT Testing
Official Title	A Prospective Registry Studyto Evaluate the Effect of the DCISionRT Test on Treatment Decisions in Patients With DCIS Following Breast Conserving Therapy
Brief Summary	This is a prospective cohort study for patients diagnosed with ductal carcinoma in situ (DCIS) of the breast. The primary objective of the study is to create a de-identified database of patients, test results, treatment decisions and outcomes that can be queried to determine the utility of the DCISionRT™ test in the diagnosis and treatment of ductal carcinoma in situ of the breast.
Study Design	Observational Model: Cohort Time Perspective: Prospective
Intervention	Diagnostic Test: DCISionRT - The Prelude DCISionRT Test was developed by Prelude Corporation and is performed at its CLIA laboratory facility. The biomarkers used to evaluate the biologic signature of DCIS tissue are based on over a decade of research including the University of California, San Francisco, Yale University as well as Prelude Corporation. The test is prognostic for 10-year recurrence risk and predicts RT treatment benefit for invasive breast cancer. The laboratory is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high-complexity clinical testing and is accredited by the College of American Pathologists (CAP).
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 following eligibility criteria.
Eligibility Criteria	Inclusion criteria: • A clinical decision has been made to order the DCISionRT™ Test as part of routine patient 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 eligible for, or have already received breast conserving surgery • Patient must be eligible to receive radiation and/or systemic treatment • Patient must be female and greater than 25 years old • Patient must be able to provide informed consent Exclusion criteria: • Patient tissue is insufficient to generate DCISionRT test results or required DCISionRT inputs (age, tumor size, margin status, palpability) are missing • Patient has invasive breast cancer or evidence in the ipsilateral or contralateral breast of invasive breast cancer, including microinvasion, lymph node involvement, or Paget's disease of the nipple • Patient has already been surgically treated with a mastectomy for primary DCIS • Patient has prior in situ or invasive breast cancer

Protocol Synopsis, continued	
Study Groups/ Cohorts	Ductal Carcinoma In Situ (DCIS) Patients must have histologically confirmed ductal carcinoma in situ (DCIS) in a single breast without evidence of invasive cancer (presence of lobular carcinoma in situ (LCIS) or other benign breast disease in addition to DCIS is acceptable).
Primary Outcome Measures	Percent of Cases with Changes in Treatment Recommendation [Time Frame: 5 years] 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, therapeutic mastectomy, contralateral prophylactic mastectomy), type of radiation therapy (none, IORT, APBI, whole breast RT) and endocrine therapy (yes, no). The main measure will be percent of cases in which treatment recommendations are changed after the test results become available.
Secondary Outcome Measures	Function of Demographic Factors [Time Frame: 5 years] Percent of patients for which the recommended treatments change after DCISionRT results are known as a function of demographic factors (age groups <40, 40-50 and >50; ethnicity; family history) Function of Tumor Factors [Time Frame: 5 years] Percent of patients for which the recommended treatments change after DCISionRT results are known as a function of tumor factors (tumor size, grade, architecture, necrosis, palpability, surgical margins, hormone receptor status).
Other Pre-specified Outcome Measures	Distribution of DCISionRT scores across the cohort [Time Frame: 5 years] Each patient will receive the following results from the DCISionRT test: Risk Score (0 - 10.0), Risk Category Low (<=3.0) or Elevated (>3.0), Risk Prognosis with Breast Conserving Therapy Alone (0 - 40%) and Risk Prognosis with Breast Conserving Therapy and Radiation (0 - 40%). Function of Geographic Region [Time Frame: 5 years] Percent of patients for which the recommended treatments change after DCISionRT results are known as a function of the geographic region of the investigator.
Status	Recruiting
Enrollment Target	1500
Start Date	July 2, 2021
Est. Completion	May 2034 (Final data collection date for primary outcome measure)
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Responsible Party	PreludeDx
Study Sponsor	PreludeDx
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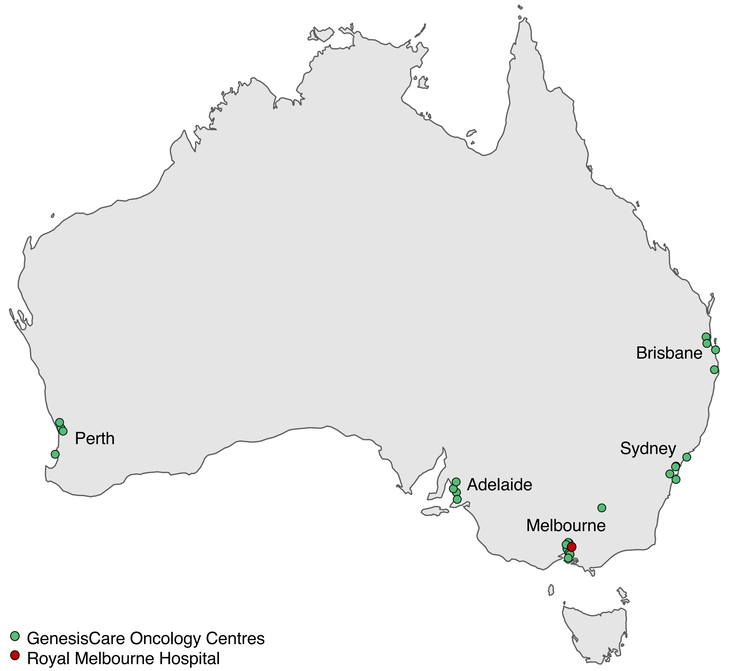
Publications	Bremer T, et. al, Clin Cancer Res 2018 Dec 1;24(23):5895-5901; PMID: 30054280 Weinmann, et. al, Clin Cancer Res 2020 Aug 1;26(15):4054-4063; PMID: 32341032 Shah C, et. al, Ann Surg Oncol. 2021 Oct;28(11):5974-5984; PMID: 33821346



All Patients Consented	Patients
Screening Failure	2
Withdrawn	0
On Study	95
Completed	9
Total Consented	**106**

Current Sites Registered	Sites
Academic Cancer Centers	1
Regional Hospitals	0
Specialty Private Practices	40
All Sites	**41**

Physician Participation	Physicians
Surgeons	85
Radiation Oncologists	41
Medical Oncologists	0
All Investigators	**126**

Summary

- 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.