DCISionRT®

San Antonio Breast Cancer Symposium 2021

Title: The PREDICT Registry: A prospective registry to evaluate the effect of a predictive assay on treatment decisions in patients with DCIS following breast conserving therapy.

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

Methods: This is a prospective cohort study for patients diagnosed with DCIS of the breast. Treating physicians complete a treatment recommendation survey before and after receiving DCISionRT test results. Test results, treatment recommendations, patient preferences and clinico-pathologic features are stored in a de-identified registry for participating institutions from a variety of geographic regions across the US. The study will also collect 5- and 10-year recurrence and survival data. The study includes females over age 25 who are candidates for BCS and eligible for RT and/or systemic treatment with sufficient tissue to generate test results. Subjects must not have been previously treated for DCIS or have previous or current invasive or micro-invasive breast cancer. 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 other clinico-pathologic factors. Changes in treatment recommendations will be assessed using McNemar's test with an alpha level of 0.05. Differences in recurrence-free and over all survival will be evaluated by Kaplan-Meier survival analysis using the log-rank test and/or the Cox Proportional Hazards model. A planned early interim analysis based on the first 200 patients has been recently completed and reported.

Results: As of July 9, 2021, 1,986 patients have been accrued from 64 institutions. Ten additional institutions are currently in the process of joining the study. We are planning to enroll up to 2,500 patients from up to 100 institutions.

Authors:

Steve Shivers, PhD
PreludeDx, Laguna Hills, CA

Troy Bremer, PhD
PreludeDx, Laguna Hills, CA

Pat W. Whitworth, MD
Nashville Breast Center, Nashville, TN

Charles Cox, MD
University of South Florida, Tampa, FL

Rakesh Patel, MD
Good Samaritan Cancer Center, Los Gatos, CA

The PREDICT Registry: A prospective registry study to evaluate the effect of the DCISionRT test on treatment decisions in patients with DCIS following breast conserving therapy

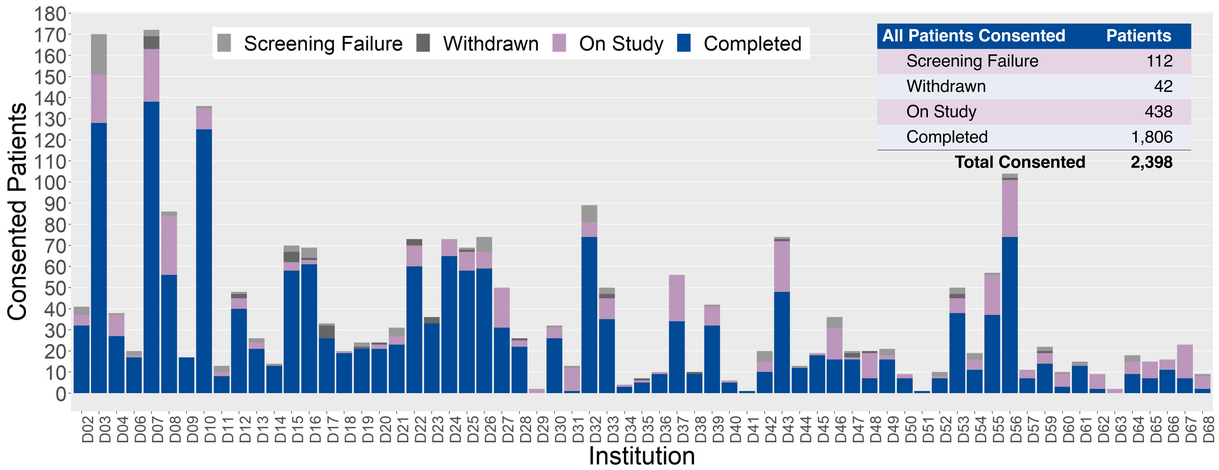
SC Shivers[1], P Whitworth[2], R Patel[3], T Bremer[1], CE Cox[4]

[1]PreludeDx, Laguna Hills, CA, [2]Nashville Breast Center, Nashville, TN, [3]Good Samaritan Cancer Center, Los Gatos, CA, [4]University of South Florida, Tampa, FL, USA

Protocol Synopsis	
NCT Number	NCT03448926
Brief Title	The PREDICT Registry
Official Title	A Prospective Registry Study to 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	Prospective Observational Cohort [Patient Registry]
Intervention	Diagnostic Test: DCISionRT - The DCISionRT Test was developed by PreludeDx (Laguna Hills, CA) 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: • 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 have the DCISionRT Test ordered during routine patient care • Patient must be planning to undergo breast conserving surgery • Patient must be eligible to receive radiation and/or systemic treatment • Patient must be greater than 25 years old • Patient must have been diagnosed with DCIS within 120 days of consent • 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 evidence of invasive breast cancer, including microinvasion, lymph node involvement, or Paget's disease of the nipple or suspicious mammogram findings in the lymph nodes or contralateral breast • Patient has been surgically treated with a mastectomy for primary DCIS • Patient has prior in situ or invasive breast cancer • Patient is pregnant

Protocol Synopsis, continued	
Study Groups/ Cohorts	Female patients with DCIS, 25 years and older. 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 w/ Changes in Treatment Recommendation [Time: 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	2500
Start Date	February 27, 2018
Est. Completion	February 2022 (Final data collection date for primary outcome measure)
Contacts	Steven C Shivers, PhD 813-215-1749 sshivers@usf.edu
Responsible Party	University of South Florida
Study Sponsor	PreludeDx
Lead Investigators	Charles E Cox, MD — University of South Florida — Tampa, FL Rakesh R Patel, MD — Good Samaritan Hospital — Los Gatos, CA Pat Whitworth, MD — Nashville Breast Center — Nashville, TN
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

Figure 1. Patients Enrolled by Institution.

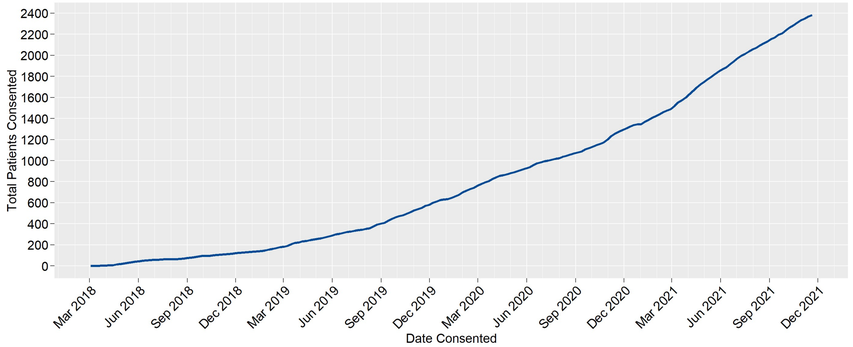


All Patients Consented	Patients
Screening Failure	112
Withdrawn	42
On Study	438
Completed	1,806
Total Consented	**2,398**

Current Sites Registered	Sites
Academic Cancer Centers	21
Regional Hospitals	35
Specialty Private Practices	11
	67

Physician Participation	Physicians
Surgeons	147
Radiation Oncologists	215
Medical Oncologists	33
	395

Figure 2. Cumulative Number of Patients Enrolled by Quarter



Summary

- The PREDICT Study has consented 1,847 women.
- There are 65 sites enrolled and about 5 sites are pending activation. The goal is to activate up to 100 sites and consent 2,500 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.
- Similar DCISionRT PREDICT registries are planning to open soon in Australia and Europe.