CanAssist Breast predicts 10-year breast cancer recurrences-Data from TEAM trial, a large multi-country prospective randomized trial

This is a study undertaken by OncoStem Diagnostics in collaboration with Leiden University Medical Centre, The Netherlands

Background: Many of the hormone receptor positive (estrogen receptor/progesterone receptor), HER2/neu negative early-stage breast cancer (EBC) patients have good prognosis with endocrine therapy alone without the need of chemotherapy. However, compared to triple negative breast cancer patients, these patients have sustained risk of recurrence until a period of 15-20 years since the disease diagnosis.[1] Large randomized clinical trials, NSABP-14 and NSABP-20 involving thousands of patients have shown that the likelihood of distant recurrence in patients who received tamoxifen for 5 years after surgery is about 15% at 10 years in node negative disease thus showcasing that not all patients benefit from chemotherapy.[2-4]

Prognostic tests have been used to segregate the hormone receptor positive, HER2/neu negative EBC patients and to limit use of chemotherapy to the ~15% of patients who will get benefitted with chemotherapy. Although multi-gene tests are well accepted and used widely in the West, they are not easily available for Asian patients. Lack of extensive validation data on Asian patients and the prohibitive cost limit the use of these multigene tests for Asian women and in under resourced regions across the globe.

We have developed CanAssist Breast (CAB)- a 'clinically relevant' and extremely 'cost effective' multi-biomarker prognostic test on 'Asian' patients. It couples 'immunohistochemistry' with cutting edge 'Artificial Intelligence (AI) generated risk score' to segregate patients into 'low or high' risk for distant recurrence.

CAB uses data from immunohistochemical stainings of five critical biomarkers (CD44, N-Cadherin, pan-Cadherin, ABCC4 and ABCC11) and couples it with 3 key clinical parameters (tumor grade, size and node status) to generate a risk score for predicting distant recurrence using an AI based statistical model. Risk score segregates patients into either low-risk or high risk for distant recurrence in 5 years from diagnosis.[5]

CAB has been in use for treatment planning in the Indian subcontinent, UAE and Turkey for the past 5 years and has helped ~2000 patients to plan optimal treatment from these cost conscious self-paid markets.

Results/ Data:

CanAssist Breast: Distant recurrence risk prediction in 5 years from diagnosis

CAB has been showcased to predict risk of distant recurrence within five years of diagnosis robustly in patients from India, USA, multiple countries in Europe on over 3000 samples. The risk stratification is significant in total cohort (treated with chemotherapy and endocrine therapy) and in a sub-cohort of patients treated with endocrine therapy alone (Figure 1A, 1B).

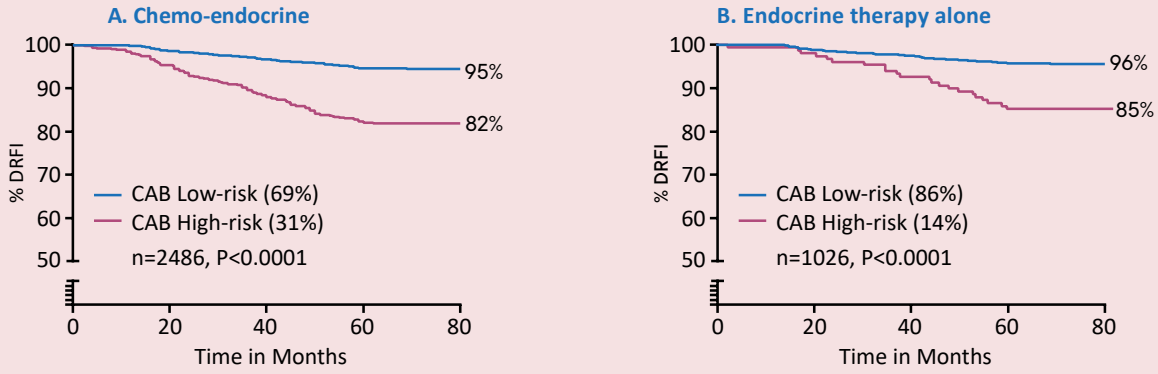

Figure 1: CAB risk stratification in total cohort: Kaplan-Meier survival curves for total cohort treated with endocrine therapy and chemo-endocrine therapy (A), endocrine therapy alone (B)

Usefulness of CAB in young, node positive breast cancer patients

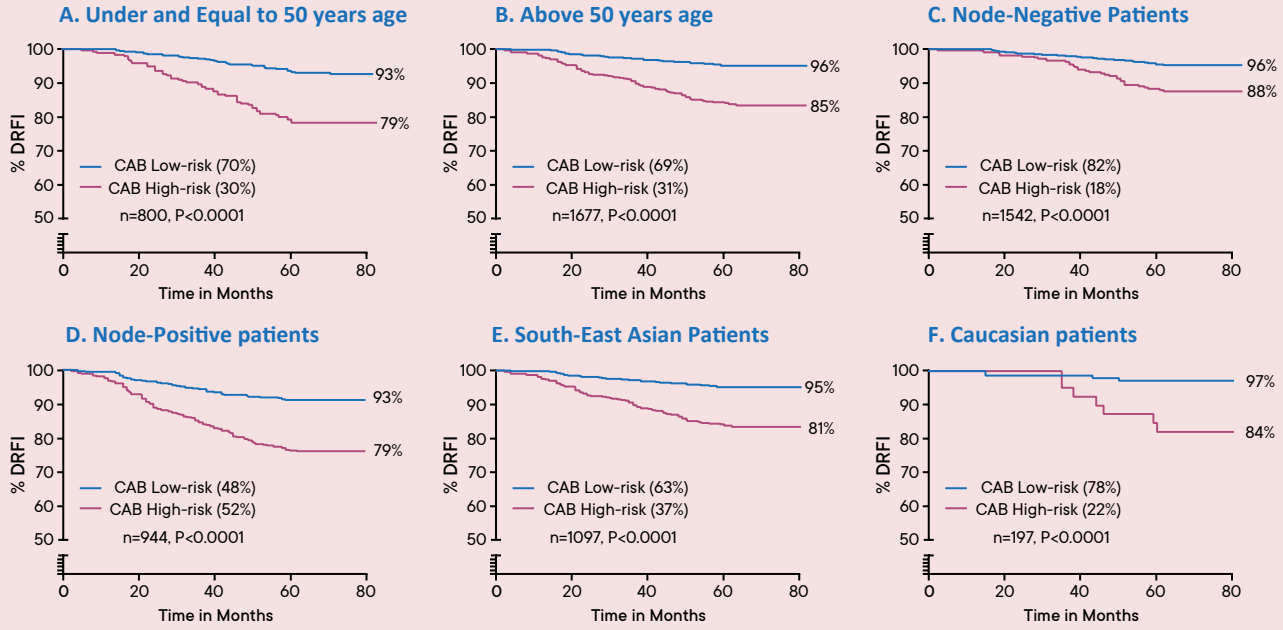

Figure 2: CAB risk stratification in sub-groups: Kaplan-Meier survival curves: In patients aged under and equal to 50 years (A), aged above 50 years (B), node-negative (C), node-positive (D), South-East Asian patients (E), Caucasian patients (F)

Additionally, in various sub-group analysis in patients' groups aged above and under 50 years, in patients with node negative tumors and node-positive tumors and in patients from South-East Asia and USA, Europe (Caucasians) CAB risk stratification was significant demonstrating that CAB performance is unaltered in various clinical sub-groups and in patients of various races/ethnicities (Figure 2A-E).[6,7]

CAB has been benchmarked with Oncotype DX[8] and MammaPrint to showcase ~ 85% concordance with Oncotype DX and MammaPrint in predicting low risk category of patients, which is much higher in comparison to the concordance showed in OPTIMA prelim trial between other genomic tests (Table 1).[9]

	Low-risk concordance
Oncotype DX vs CAB	83%
MammaPrint vs CAB	85%

Table 1: Low-risk concordance between multi-gene tests and CAB

TEAM trial: CanAssist Breast predicts distant recurrences in 10 years from diagnosis

CanAssist Breast's 10 years recurrence risk predictions were assessed in a sub-cohort of patient samples who participated in a clinical trial, TEAM conducted at The Netherlands.

TEAM (tamoxifen, exemestane adjuvant multinational) trial is a large multi-country prospective randomized clinical trial with more than 12 years of patient follow-up on clinical outcomes. The trial enrolled 9766 post-menopausal patients from 9 countries.[10] Randomization was for the use of hormonal therapy, sequential (2-3 years Tamoxifen +3-2 years Exemestane) or exemestane alone (5 years). CAB's performance was assessed in 480 TEAM samples preserved at LUMC, Netherlands. Our study cohort had 2/3rd patients with node-positive (67%) disease, 55% of cohort had tumors greater than 2cm (T2) and 28% of the cohort had poorly differentiated tumors (G3). 78% of the cohort was treated with hormonal therapy alone, either exemestane alone or tamoxifen followed by exemestane for a period of 5 years and patients were followed up for a total period of 10 years (median follow up=10.4 years).

CanAssist Breast stratified 68% of cohort as low-risk and 32% as high-risk with a low-risk DRFI (distant relapse free interval) of 86% at 10 years. In node-positive sub-cohort, the risk proportions were 63:37 with low-risk DRFI of 88% at 10 years, with a hazard ratio (HR) of 2.82 (1.66-4.89, P<0.0001) (Figure 3).

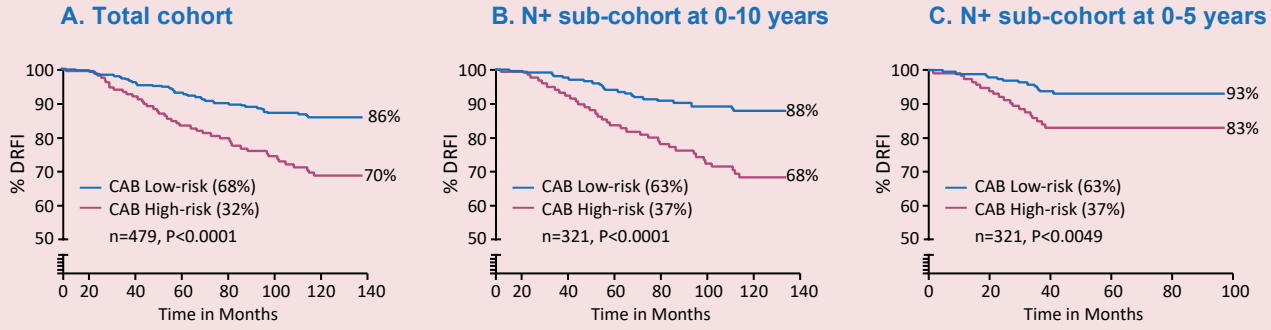

Figure 3: CAB risk stratification in total cohort: Kaplan-Meier survival curves at 10 years since the time of randomization in total cohort (A), node-positive sub-cohort (B), node-positive cohort at 5 years (C)

Following this, we looked at CAB's performance in each arm of the trial. In both the arms (sequential and exemestane) the risk stratification was significant (Figure 4). The 10-year low-risk DRFI was 82% (HR: 1.76, 0.9-3.3, P=0.05) in sequential arm and 89% in exemestane arm (HR: 3.3, 1.7-6.5, P<0.0001) (Figure 4). The CAB high risk patients showed a chemotherapy benefit with 14% of improved DRFI but not the CAB low-risk patients (Figure 5).

This exciting data from a prospective TEAM trial shows the usefulness of CAB for long term (10-year) predictions of recurrence risk in early-stage hormone receptor positive, HER2/neu negative breast cancer.

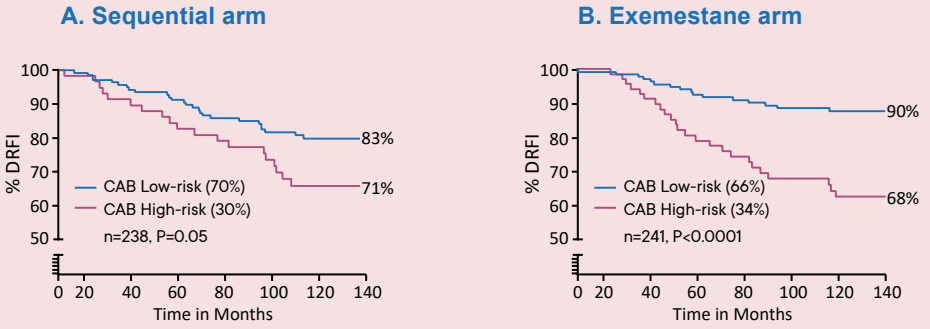

Figure 4: CAB risk stratification across both the arms of hormonal therapy: Kaplan-Meier survival curves at 10 years since the time of randomization in sequential arm (A), exemestane arm (B)

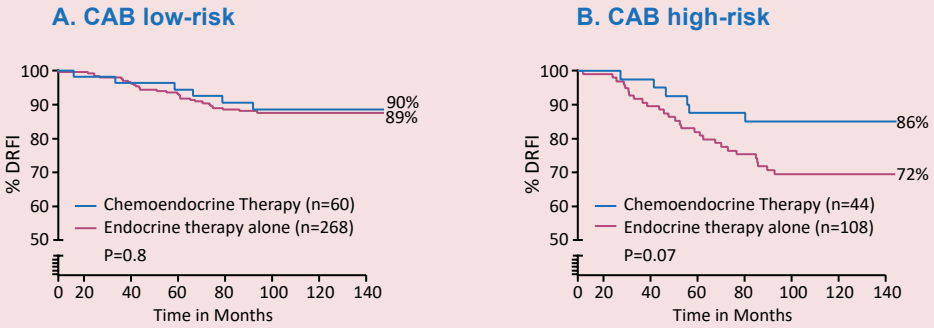

Figure 5: Chemotherapy benefit in CAB stratified patients: Kaplan-Meier survival curves in CAB low-risk (A), CAB high-risk (B)

Conclusions from TEAM trial:

This data for the first time shows that CanAsssist Breast can reliably predict risk of distant cancer recurrence up to 10 years from diagnosis and is predictive of chemotherapy benefit in high-risk patients.

This data is exciting as CAB low risk DRFI (93%) is comparable to the DRFS shown in post-menopausal women with node-positive disease with chemotherapy (91.9%) or without chemotherapy (91.6%) having Oncotype DX RS between 0-25 as per RxPonder trial. [11]

Thus, this TEAM validation data from prospective clinical trial along with earlier data from numerous retrospective cohorts from various geographies reinforce the utility of CAB in prognostication of breast cancer patients across global population.

References:

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