OncoStem
*redefining cancer treatment*
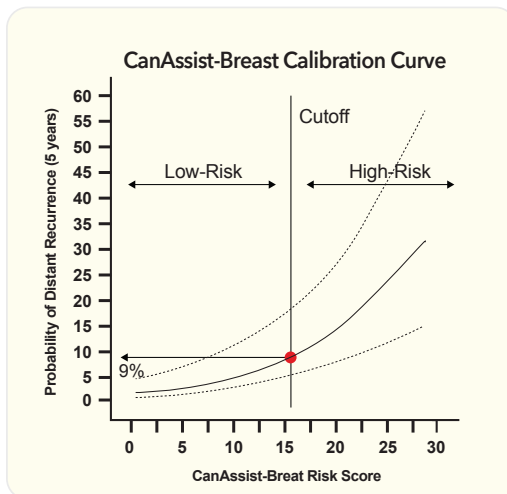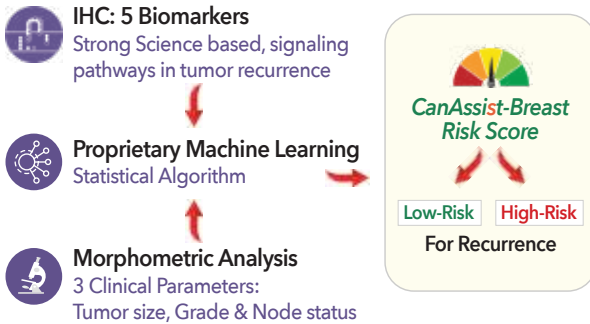
*Don't worry about cancer recurrence!*

*We can assist with CanAssist*

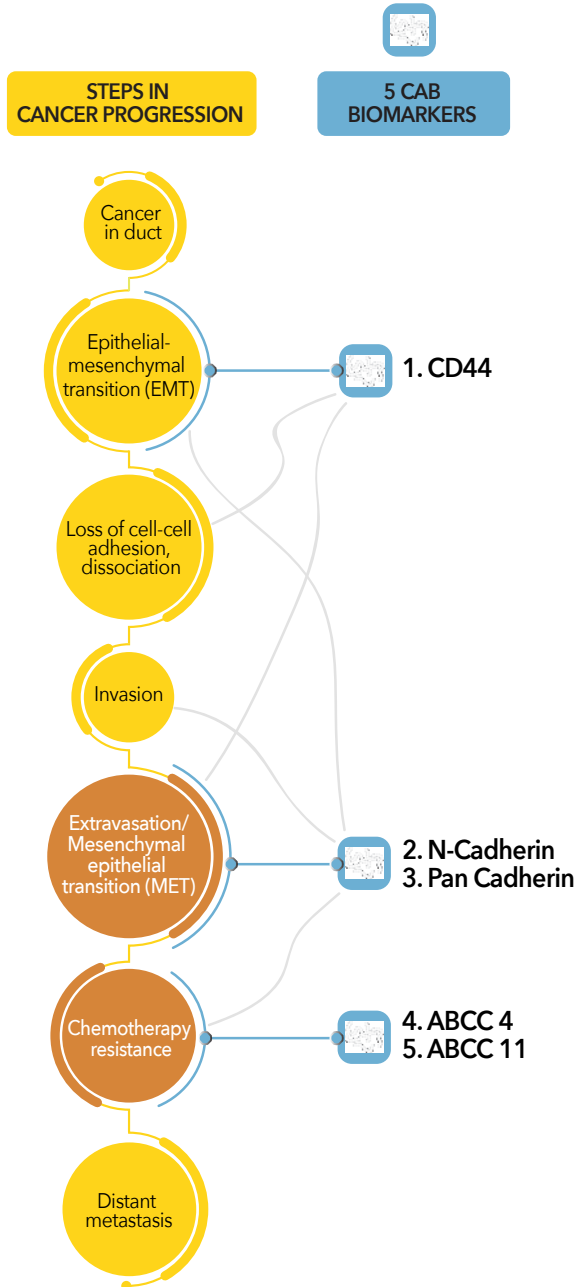## CanAssist-Breast

**redefining cancer treatment doctors**

# Risk Prediction using
# *CanAssist-Breast*

Machine learning-based test that stratifies breast cancer patients based on risk of recurrence. CanAssist-Breast integrates IHC data and clinical parameters into a statistical algorithm which provides CanAssist-Breast (CAB) score that stratifies patients as "low-risk" or "high-risk" for distant recurrence over 5 years

**IHC: 5 Biomarkers**
Strong Science based, signaling pathways in tumor recurrence

**Proprietary Machine Learning**
Statistical Algorithm

**Morphometric Analysis**
3 Clinical Parameters:
Tumor size, Grade & Node status

*CanAssist-Breast Risk Score*

Low-Risk    High-Risk

**For Recurrence**

## CanAssist-Breast Calibration Curve

Cutoff

Low-Risk          High-Risk

9%

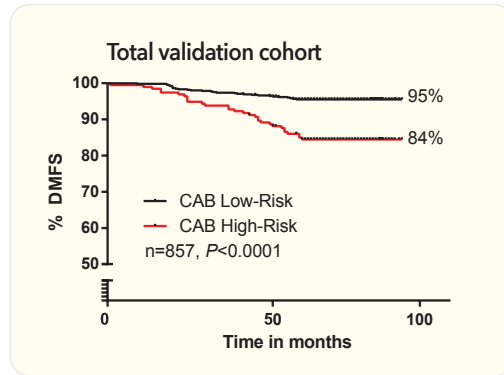Probability of Distant Recurrence (5 years)

CanAssist-Breat Risk Score

CanAssist-Breast Risk Scores are directly proportional to probability of distant recurrence. The CanAssist-Breast Risk Score cut-off of 15.5 corresponds to a 9% probability of distant recurrence
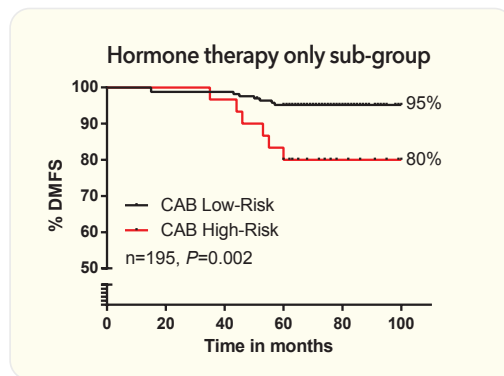
# CanAssist-Breast assesses expression of unique biomarkers that play critical roles in metastasis



**STEPS IN CANCER PROGRESSION**

**5 CAB BIOMARKERS**

- Cancer in duct
- Epithelial-mesenchymal transition (EMT) — 1. CD44
- Loss of cell-cell adhesion, dissociation
- Invasion
- Extravasation/ Mesenchymal epithelial transition (MET) — 2. N-Cadherin / 3. Pan Cadherin
- Chemotherapy resistance — 4. ABCC 4 / 5. ABCC 11
- Distant metastasis

### Total validation cohort



**% DMFS** vs **Time in months**

95%

84%

CAB Low-Risk
CAB High-Risk
n=857, *P*<0.0001

- CanAssist-Breast identifies distinct groups of low-risk and high-risk patients in Kaplan-Meier survival analysis
- The low-risk group has <5% rate of distant recurrence

### Hormone therapy only sub-group



**% DMFS** vs **Time in months**

95%

80%

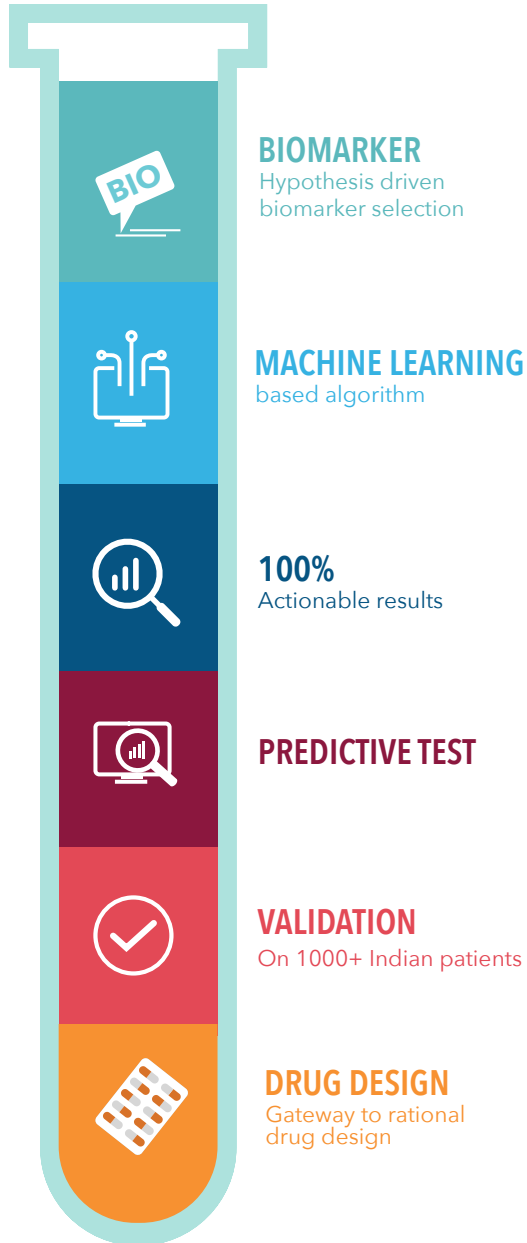CAB Low-Risk
CAB High-Risk
n=195, *P*=0.002

- CanAssist-Breast is significantly prognostic in a cohort treated with endocrine therapy alone
- Validation in endocrine therapy alone treated cohort gives you the confidence that CAB provides accurate risk predictions
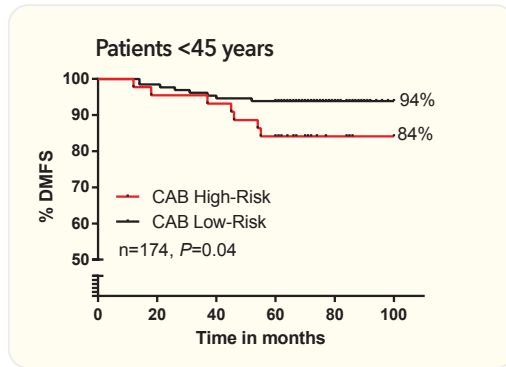
## *CanAssist-Breast is a significant predictor of prognosis*

# CanAssist-Breast



**BIOMARKER**
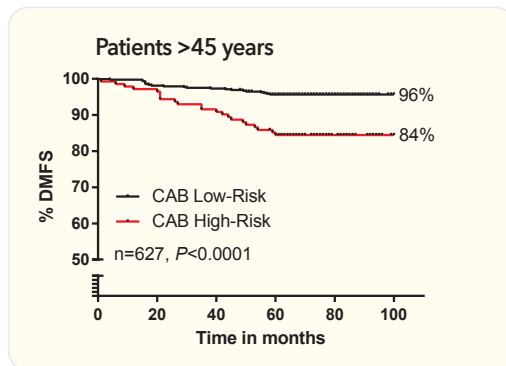Hypothesis driven
biomarker selection

**MACHINE LEARNING**
based algorithm

**100%**
Actionable results

**PREDICTIVE TEST**

**VALIDATION**
On 1000+ Indian patients

**DRUG DESIGN**
Gateway to rational
drug design

# CanAssist-Breast is prognostic in younger patients



**Patients <45 years**

- % DMFS (y-axis: 50–100)
- Time in months (x-axis: 0–100)
- CAB High-Risk
- CAB Low-Risk
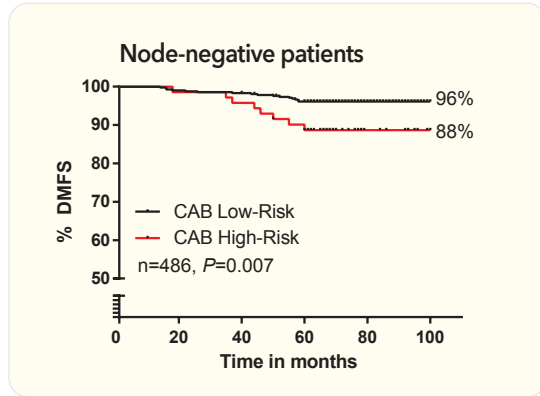- n=174, *P*=0.04
- 94%
- 84%

- CanAssist-Breast has been validated on patients across all age groups
- It can stratify younger patients into low-risk and high-risk groups as effectively as it can stratify older patients.
- This is important because the mean age of diagnosis of breast cancer in Asia is a decade earlier than the West
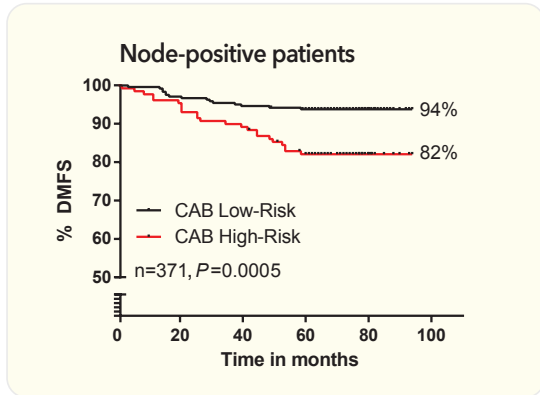


**Patients >45 years**

- % DMFS (y-axis: 50–100)
- Time in months (x-axis: 0–100)
- CAB Low-Risk
- CAB High-Risk
- n=627, *P*<0.0001
- 96%
- 84%

# CanAssist-Breast is an independent predictor of prognosis

| Covariate | Hazard ratio | *p*-value | 95% CI |
|---|---|---|---|
| Age | 1.55 | 0.09 | 0.92-2.61 |
| ER | 1.12 | 0.75 | 0.55-2.25 |
| PR | 1.67 | 0.04 | 1.0-2.80 |
| CT treatment | 1.38 | 0.30 | 0.74-2.58 |
| CanAssist-Breast risk score | 3.39 | <0.0001 | 2.05-5.61 |

# CanAssist-Breast is prognostic independent of node status

## Node-negative patients



% DMFS vs Time in months

- CAB Low-Risk — 96%
- CAB High-Risk — 88%

n=486, *P*=0.007

- 5-year distant recurrence was <4% for low-risk patients

## Node-positive patients



% DMFS vs Time in months

- CAB Low-Risk — 94%
- CAB High-Risk — 82%

n=371, *P*=0.0005
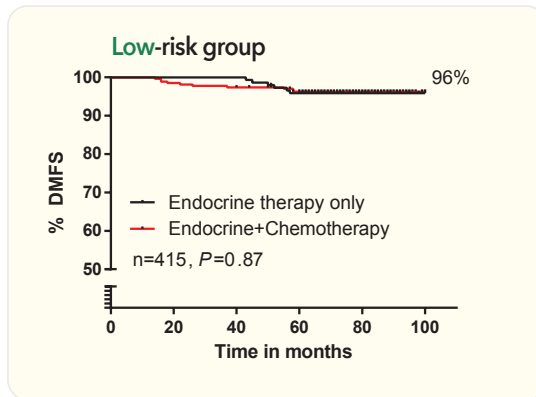
- 65% of node-positive patients- a population that routinely receives chemotherapy- were classified as low-risk by CAB and had recurrence rates <6%

# CanAssist-Breast is predictive of "Chemotherapy Benefit"



**Low-risk group**

% DMFS vs Time in months

— Endocrine therapy only
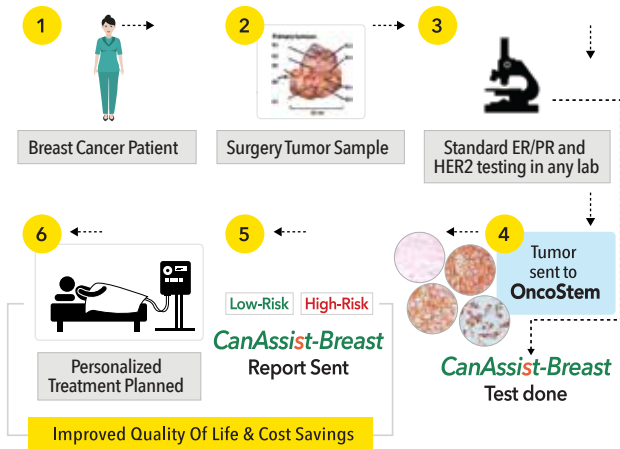— Endocrine+Chemotherapy
n=415, *P*=0.87

96%

- No difference in DMFS for low-risk patients who are given adjuvant chemotherapy plus endocrine therapy vs those given only endocrine therapy
- Insignificant benefit from chemotherapy to patients called low-risk by CanAssist-Breast



**High-risk group**

% DMFS vs Time in months

— Endocrine therapy only
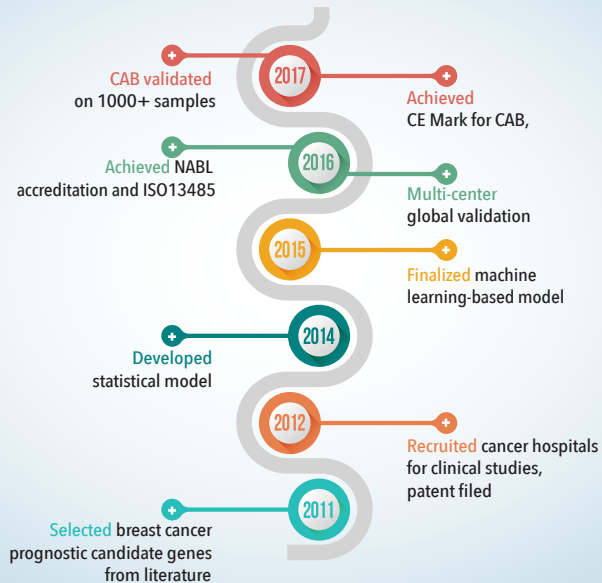— Endocrine+Chemotherapy
n=71, *P*=0.02

94%
75%
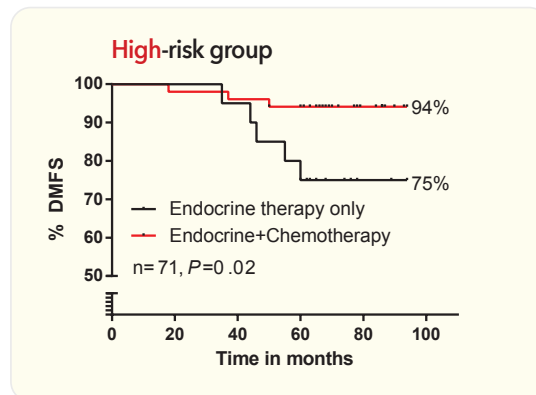
- CAB provides 19% chemotherapy benefit for high-risk patients who take adjuvant chemotherapy plus endocrine therapy vs those who take only endocrine therapy

# Workflow of CanAssist-Breast Breast Testing

1. Breast Cancer Patient
2. Surgery Tumor Sample
3. Standard ER/PR and HER2 testing in any lab
4. Tumor sent to **OncoStem** — *CanAssist-Breast* Test done
5. Low-Risk | High-Risk — *CanAssist-Breast* Report Sent
6. Personalized Treatment Planned

Improved Quality Of Life & Cost Savings

# CanAssist-Breast: Development Timeline

**2017**
- CAB validated on 1000+ samples
- Achieved CE Mark for CAB,

**2016**
- Achieved NABL accreditation and ISO13485
- Multi-center global validation

**2015**
- Finalized machine learning-based model

**2014**
- Developed statistical model

**2012**
- Recruited cancer hospitals for clinical studies, patent filed

**2011**
- Selected breast cancer prognostic candidate genes from literature

**OncoStem Diagnostics** performs immunohistochemical (IHC) testing as per standard guidelines for

1) Estrogen Receptor (ER)
2) Progesterone Receptor (PR)
3) HER2/neu
4) Ki67

OncoStem's laboratory is NABL accredited for IHC testing of the above-mentioned prognostic markers. OncoStem also regularly participates in External Quality Assurance Schemes (EQAS) including CAP Proficiency Testing.


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