

Abstract

Background: Data on prognostication of Asian HR+/HER2/neu- early-stage breast cancer patients using Western prognostic tests is limited and intriguing. Asian patients do get diagnosed almost a decade earlier and typically in Stage II thus the underlying tumor biology could be different. CanAssist Breast (CAB)- an immunohistochemistry and artificial intelligence based prognostic test was developed on Indian patient's tumors and validated in retrospective global studies in India, US, Spain, Germany, Austria, Italy and via prospective-randomized completed TEAM trial in The Netherlands. CAB is included in Asian geriatric Society's guidelines as well. Since mid 2016, CAB is in clinical use in India as well as Sri Lanka, Bangladesh, UAE and Turkey. In this abstract we assess the usefulness of CAB in our day-to-day treatment planning in India.

Methods: We analysed use of CAB on total 643 consecutive patients in our clinical practice from mid 2016 till December 2023. Specifically, we analyzed how does CAB segregate patients under/over 48 years ie pre/post-menopausal, N0, N1 patients. Patients with varying levels of tumor size, tumor grade and expression of ER and PR.

Results: Over-all CAB segregated 66% patients as 'low risk' and 34% as 'high risk' for distant recurrence. Median age of the patient was 58 years and median tumor size was 2.5cm. Majority (75%) of patients were over 48 years of age. The low:high risk segregation in pre- and post-menopausal was similar at 68:32 and 65:35. The current data is represented from North, South and West of India and in each of the regions as well the distribution of low:high risk proportions was similar. 33% patients had T1 tumors, 63% had T2 tumors however the low: high risk proportions in T1 versus T2 were significantly different at 84:16 and 59:41 respectively. Majority (75%) of patients had lymph node negative disease (N0) and the low:high risk proportions were 75:25 and 35:65 in N0 and lymph node positive (N1) disease. G1 tumors represented 12% of the total while 64% were G2 and 24% had G3 tumors. Low risk percentage across the three tumor grades was significantly different at 92%, 77% and 24% respectively. 88% of patients had ER and PR positive disease while 5% had ER+/PR- disease and for 7% PR status was unknown. 88% of patients had high ER expression (>70%) while 10% had intermediate (10-70%) and 1% had low ER (1-9%) expression. 46% patients had T2N0, 27% had T1N0, 7% had T1N1 and 17% had T2N1 disease. 99% were HER2/neu negative. CAB was used to plan treatment for all of these patients. We have treatment details for 77% of the patients. 94% of low-risk patients did not get chemotherapy and 84% of high-risk patients got chemotherapy. For the 6% low-risk patients who got chemotherapy, we believe the potential reasons could be N1 disease, G3 disease, high Ki67 index, Her2+ disease and pre-menopausal patients.

Conclusion: CAB is able to segregate the patients into low or high risk in line with clinical parameters. CAB has helped 94% of low-risk patients to avoid chemotherapy. CAB represents tumor biology of younger patients and coupled with world-wide validation it presents as a cost-effective, ideal alternative to western prognostic tests to patients in Asia.

Introduction

- CAB is an immunohistochemistry based prognostic test performed on FFPE breast tumors to predict the risk of distant cancer recurrence within 5 years of diagnosis for patients with hormone receptor-positive, Her2-negative (HR+/HER2-) early breast cancer (EBC).
- Based on the risk of recurrence, CAB assesses who will 'need/benefit from' chemotherapy and helps to reduce the 'over-treatment' of HR+/HER2- EBC patients with chemotherapy.
- CAB has been in use for last 8 years in India and select countries internationally.

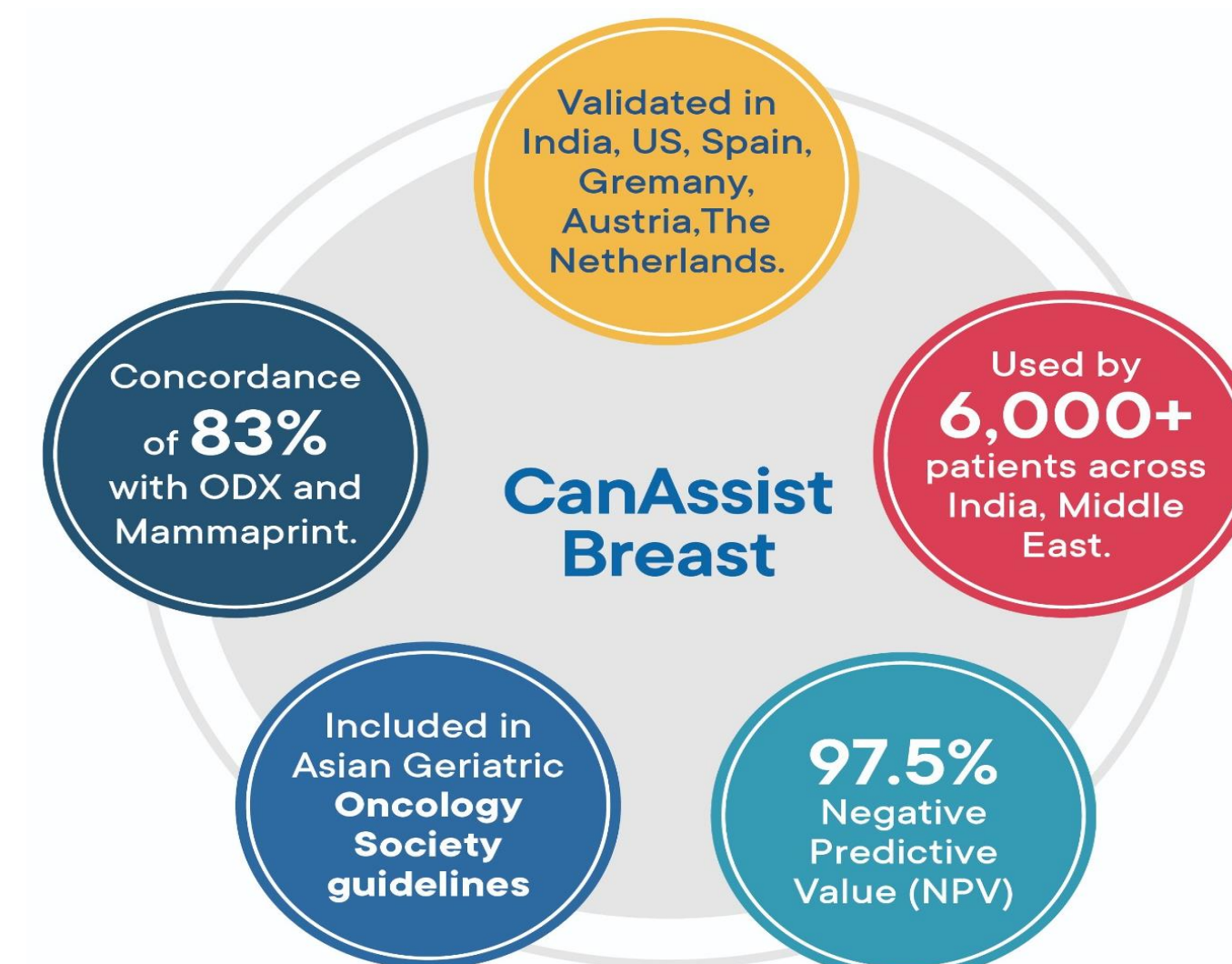


Figure 1: Key highlights of CanAssist Breast Test (CAB)

Aim

The aim of this study is to evaluate the utility of the CanAssist Breast test (CAB) in stratifying breast cancer patients in India, and its impact on chemotherapy treatment decisions by physicians.

Methodology

- 643 FFPE blocks from eligible patients diagnosed with early-stage HR+/HER2- breast cancer across five centres and were shipped to OncoStem Diagnostics, Bangalore.
- At OncoStem Diagnostics, IHC was performed for the 643 samples using automated Ventana platform and CanAssist Breast risk category was assigned using AI based algorithm.
- Data analysis was performed based on the CanAssist breast test reports.

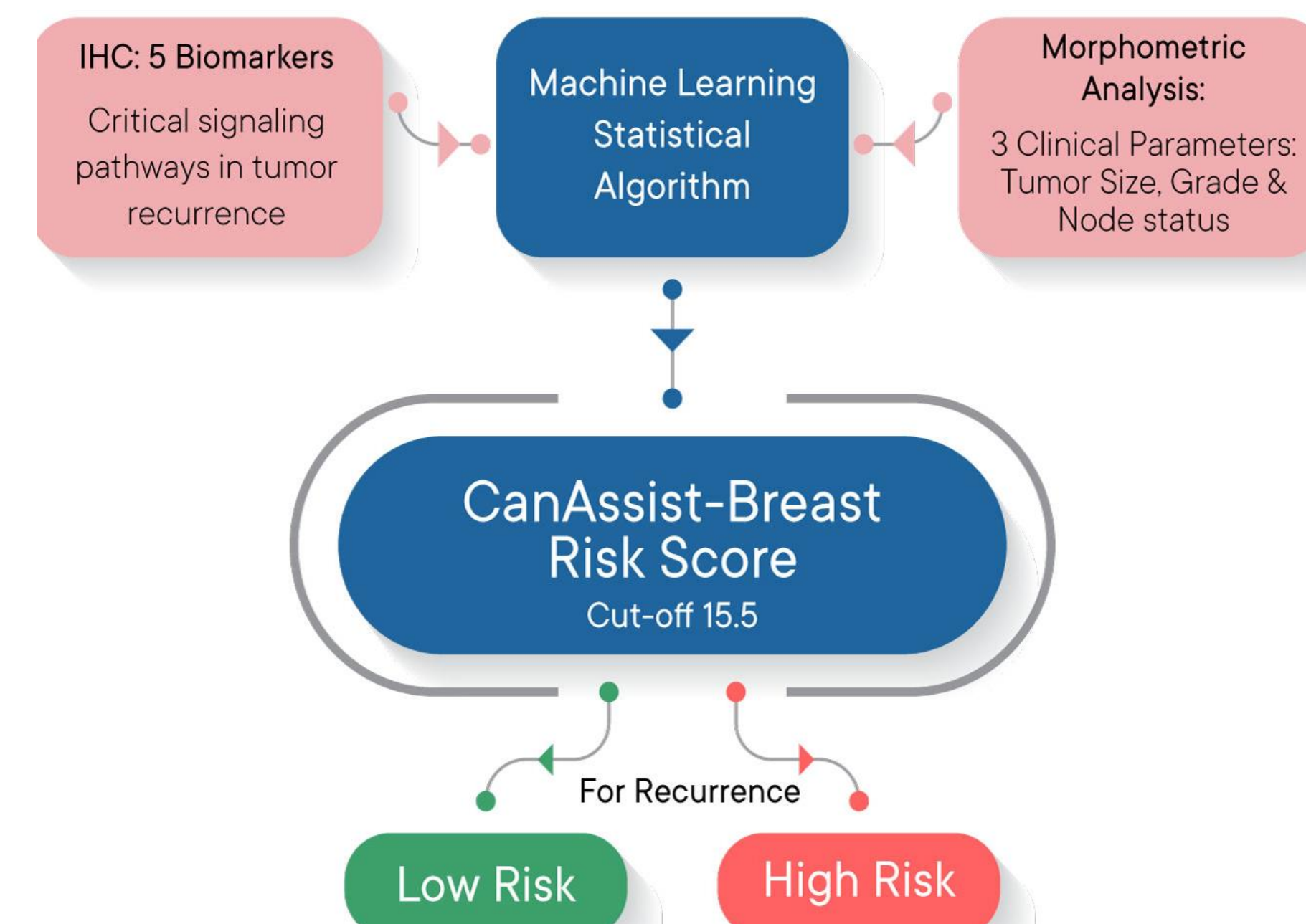


Figure 2: Generation of CAB risk score- IHC gradings of five biomarkers along with three clinical parameters are given as inputs in support vector machine algorithm to generate a risk score. Based on cut-off of 15.5, each patient is categorised as either low-risk or high-risk for recurrence

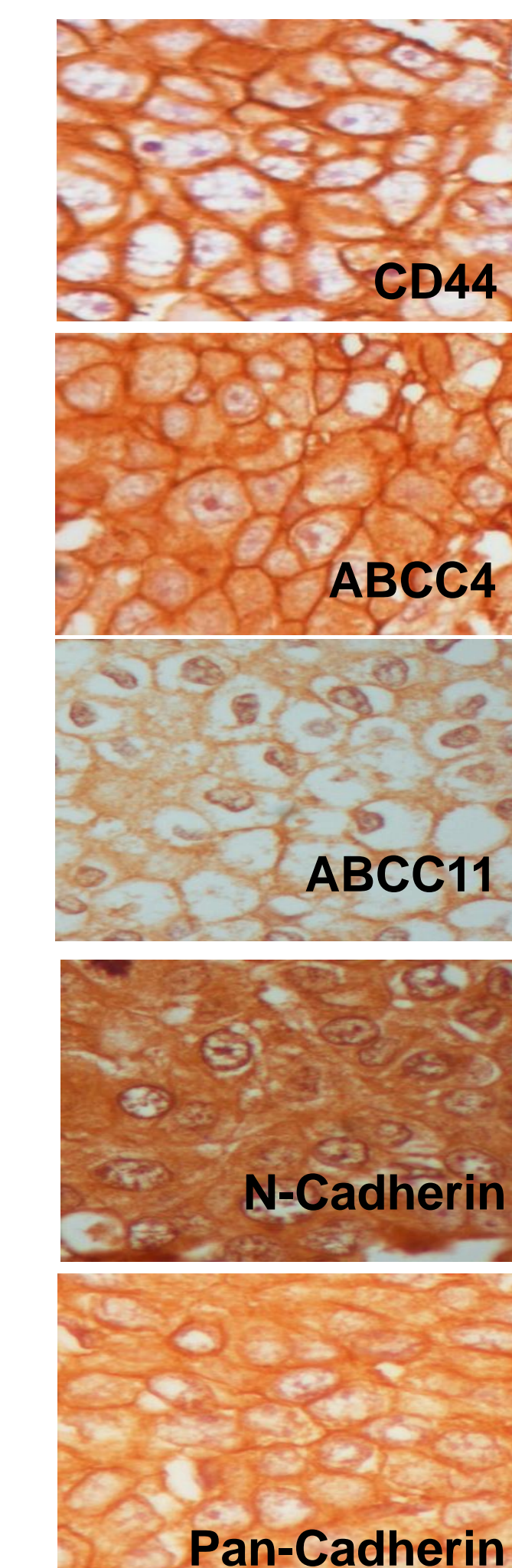


Figure 3: Representative IHC images of five CAB biomarkers

References

- Zhang X, Gunda A, Kranenbarg EM, et al. Ten-year distant-recurrence risk prediction in breast cancer by CanAssist Breast (CAB) in Dutch sub-cohort of the randomized TEAM trial. *Breast Cancer Res.* 2023 Apr 14;25(1):40.
- Gunda A, Basavaraj C, Serkad V CP, et al. A retrospective validation of CanAssist Breast in European early-stage breast cancer patient cohort. *Breast.* 2022 Jun;63:1-8.
- Dinesh Chandra Doval, Anurag Mehta, S.P. Somashekhar, et al., The usefulness of CanAssist breast in the assessment of recurrence risk in patients of ethnic Indian origin, *The Breast*, Volume 59,2021,Pages 1-7, Ramkumar C et al., Development of a Novel Proteomic Risk-Classifer for Prognostication of Patients With Early-Stage Hormone Receptor-Positive Breast Cancer. *Biomarker Insights* 2018; 13: 1-9.

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Conflict of interest

All authors have declared no conflict of Interest

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Results

Table 1: Distribution and CAB risk stratifications of patient demographics

Parameters	No. of Patients n (%)	Low risk n (%)	High risk n (%)
Total	643	422 (66%)	221 (34%)
Age	≤ 48	159 (25%)	108 (68%)
	> 48	484 (75%)	314 (65%)
	Age (Median)	58	
Gender	Female	641 (99.6%)	420 (66%)
	Male	2 (0.3%)	2 (100%)
Tumor size	T1	215 (33%)	181 (84%)
	T2	405 (63%)	240 (59%)
	T3	22 (3%)	1 (5%)
	T4	1 (0.2%)	0
	Median in cm	2.5	
Node status	Node negative (N0)	485 (75%)	366 (75%)
	Node positive (N+)	158 (25%)	56 (35%)
Histological Tumor Grade	G1	74 (12%)	68 (92%)
	G2	413 (64%)	317 (77%)
	G3	156 (24%)	37 (24%)
Hormone receptor status	ER+/PR+	568 (88%)	383 (67%)
	ER+/PR-	35 (5%)	21 (60%)
	Low ER (1 to 9%)	6 (1%)	3 (50%)
Intermediate ER (10 to 70%)	63 (10%)	45 (71%)	
	High ER (> 70%)	563 (88%)	367 (65%)

- Out of 643 patients, specific percentages of ER was not available for 11 patients and PR for 40 patients.

Figure 4:(A)TNM status distribution (%), (B)Region wise distribution in India (%)

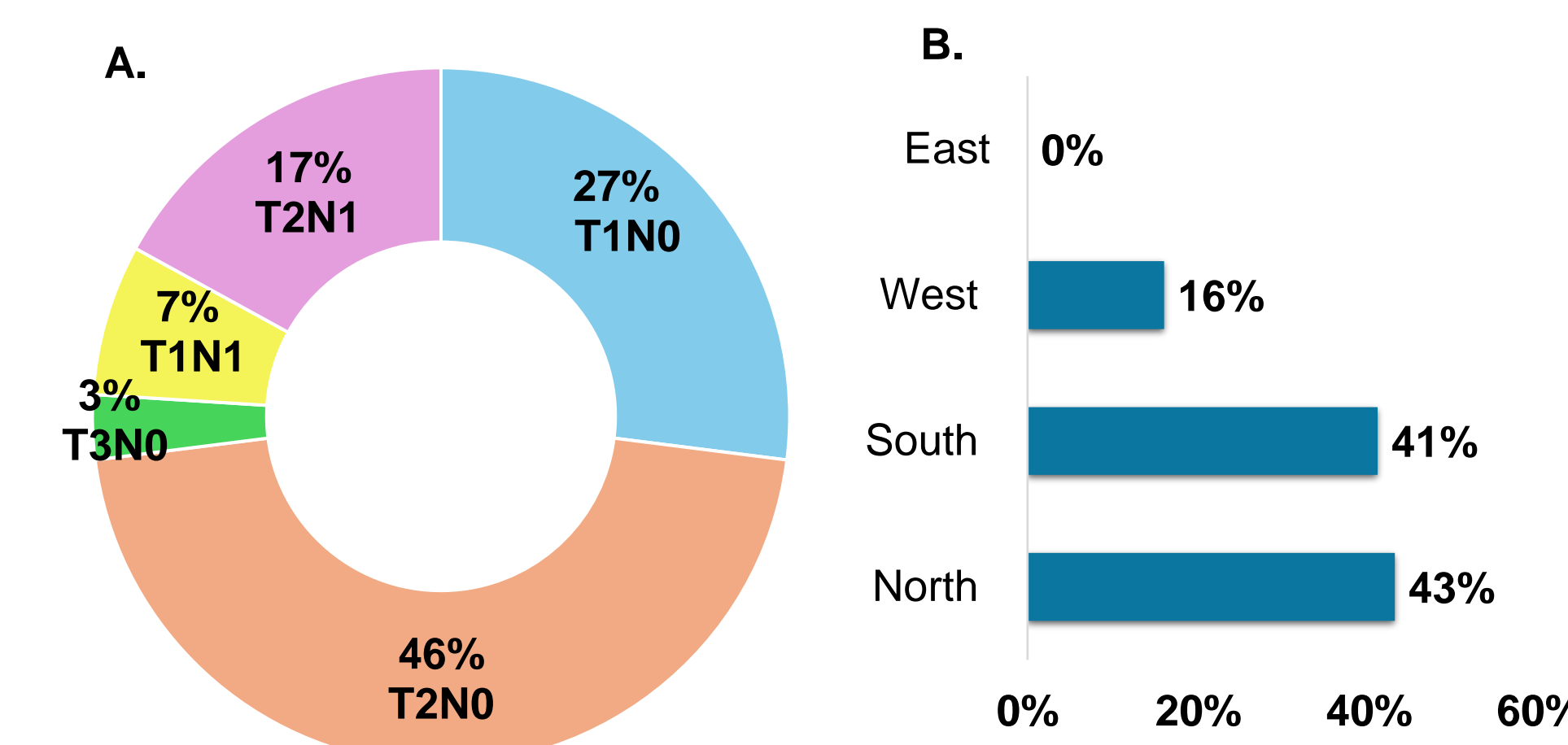
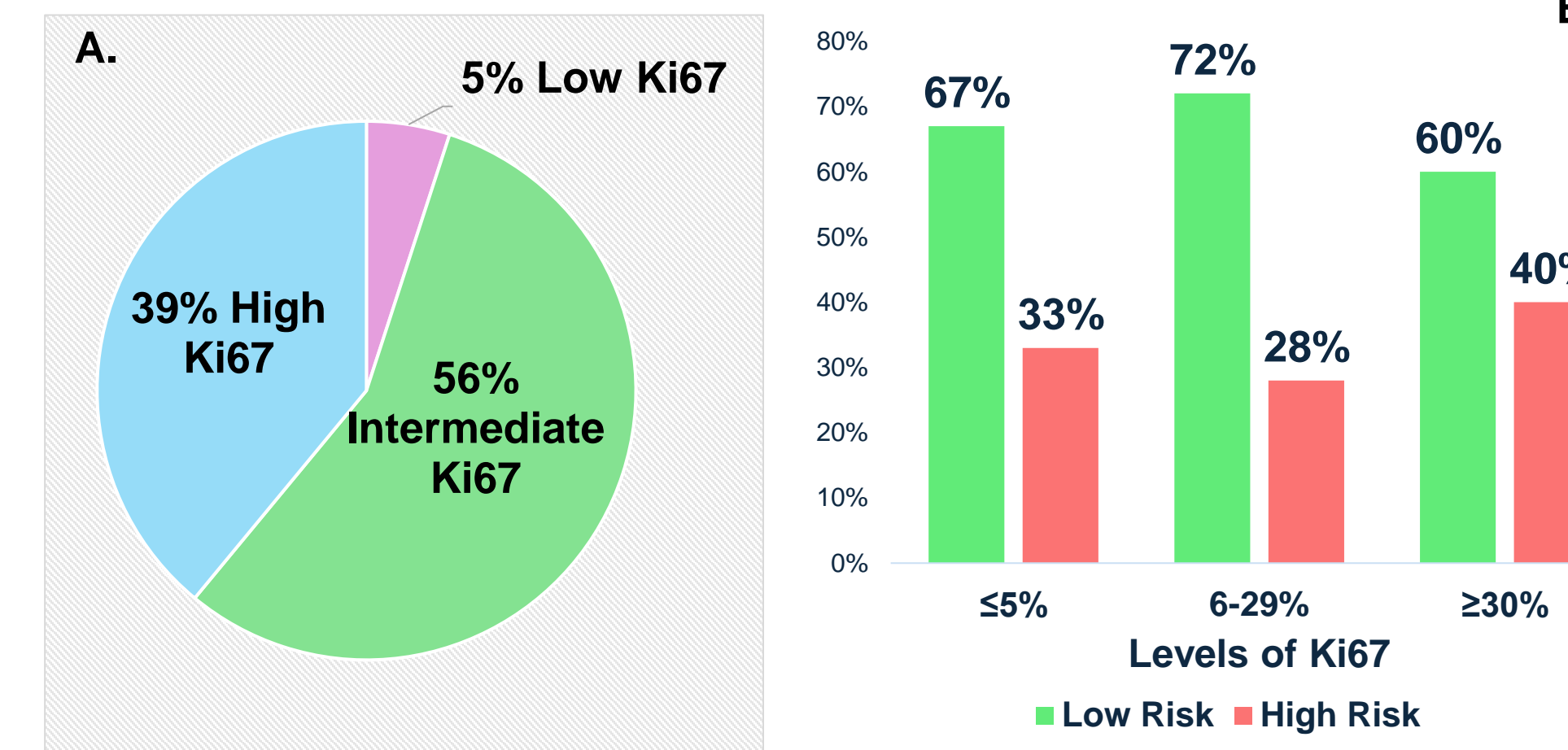


Figure 5 : (A) Ki67 distribution, (B) CAB Risk Stratification of Ki67 (%)



- Out of 643 patients, Ki67 values were available for only 457 patients.
- Ki67 distribution is represented as per The International Ki67 in Breast Cancer working group (IKWG) guidelines.

Table 2 : Adherence to CAB treatment recommendations by physicians

Category of patients	CAB risk category	n (%)	Chemo-therapy not given n (%)	Chemo-therapy given n (%)	Compliance in CAB Low-risk (%)	Compliance in CAB High-risk (%)
All patients (n=496)	Low-Risk	332(67%)	311 (94%)	21 (6%)	94%	
	High-Risk	164(33%)	26(16%)	138 (84%)		84%
N0 (n= 270)	Low-Risk	205(76)	190(93%)	159(7%)	93%	
	High-Risk	65(24)	8(12%)	57(88%)		88%
N+ (n= 122)	Low-Risk	48(39)	44(92%)	4(8%)	92%	
	High-Risk	74(61)	12(16%)	62(84%)		84%
Age ≤ 48 (n=123)	Low-Risk	87(71)	80(92%)	7(8%)	92%	
	High-Risk	36(29)	3(8%)	33(92%)		92%
Age > 48 (n=373)	Low-Risk	245(66)	231(94%)	14(6%)	94%	
	High-Risk	128(34)	229(17%)	106(83%)		83%

- Treatment follow up data was available for 496 (77%) patients.
- 94% of the low-risk patients did not undergo chemotherapy.
- 84% of high-risk patients received chemotherapy.
- Higher treatment compliance in observed in younger high-risk patients (92%) compared to other high-risk subgroups.

Conclusion

- CAB is a pioneering prognostic test developed and validated on Asian patients.
- CAB is effectively able to stratify early-stage HR+, HER2- breast cancer patients across various clinical demographics routinely seen.
- CAB effectively guided treatment decisions, with 94% of low-risk patients avoiding chemotherapy, while 84% of high-risk patients received chemotherapy
- CAB offers a cost- effective and suitable alternative to western prognostic tests to patients in Asia, Africa and ME.