

# Clinical Evaluation of Thioredoxin 1 in the Blood as a Novel Biomarker to Detect Breast Cancer

# A-210

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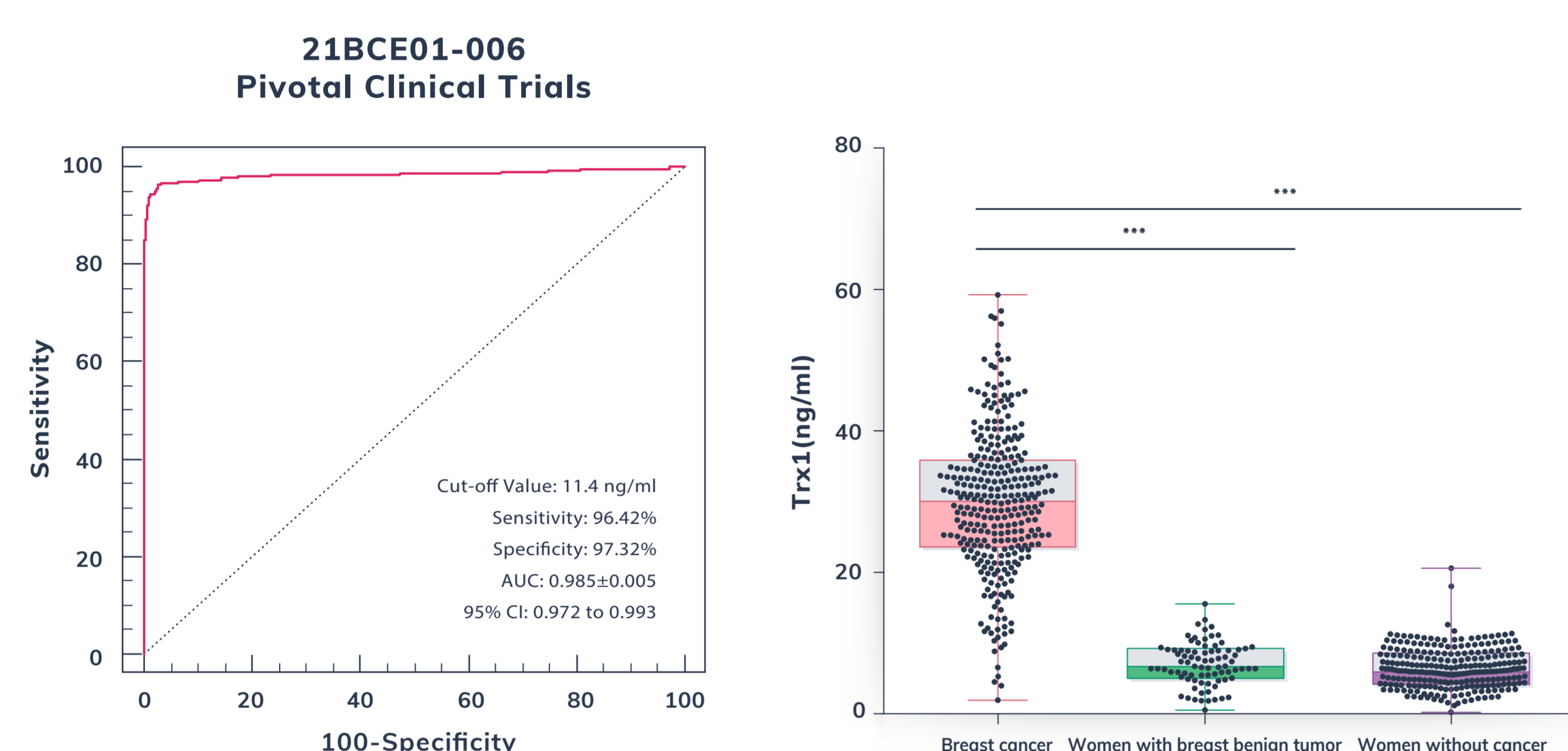
## Background & Methods

**Background:** For a long time, there has been an unmet need to find a means to detect breast cancer (BC) with blood for the mutual benefit of women and clinicians. We have reported that the serum level of thioredoxin 1 (Trx1) could be a biomarker to assess the risk of BC. This novel BC detection tool was thought to be an alternative way to improve the diagnosis accuracy of BC. A pivotal clinical trial has been performed to validate its clinical utility with support from the Promotion of Innovative Businesses for Regulation-Free Special Zones, Ministry of SMEs and Startups (MSS, Korea).

**Methods:** An ELISA kit, DxMe<sup>®</sup> BC, to estimate the level of serum Trx1 has been developed. The performance of DxMe<sup>®</sup> BC kit to assess the risk of BC was evaluated. A total of 1,032 sera have been analyzed in this pivotal clinical trial including biopsy confirmed BC patients (n=308), women without cancer or other breast related symptoms (n=336), and other malignancies (n=388) such as stomach, lung, colorectal, cervical, and ovarian cancers. The blood levels of Trx1 from various pathological and physiological status of BC patients compared to control groups were analyzed. The combined analysis of Trx1 level with mammography was performed to see how well Trx1 level could correct previously mis- or incompletely judged mammograms. All measurements were duplicated and statistically analyzed by ROC analysis, one-way ANOVA, and unpaired t-test.

## Results & Conclusions

**FIG. 1.** Clinical sensitivity and specificity of DxMe<sup>®</sup> BC test to detect breast cancer by measuring Trx1 levels in sera



The levels of blood Trx1 were estimated from 308 biopsy-confirmed BC patients, 82 breast benign tumor bearers, and 254 women without any disease (total of 336 women as a control group). Trx1 levels were analyzed by ROC analysis to calculate the clinical sensitivity and specificity. The clinical sensitivity and specificity were 96.43% and 97.32%, respectively. The AUC was 0.985 (95% CI: 0.972 to 0.993) with the cut-off value of 11.4 ng/ml.

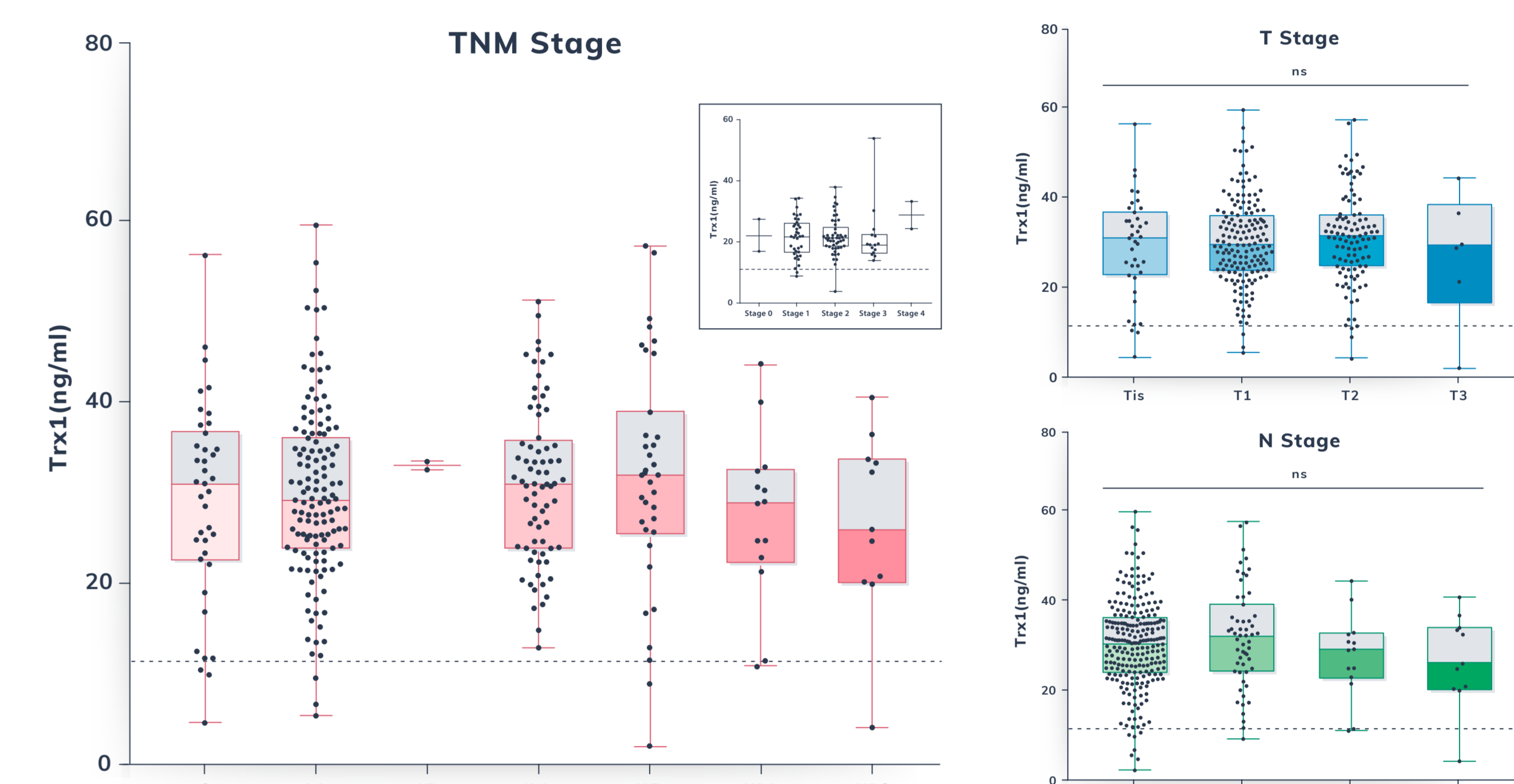
- The clinical sensitivity and specificity of blood Trx1 level test to detect BC were **96.43%** and **97.32%**, respectively (AUC 0.985).
- The level of blood Trx1 could differentiate BC regardless of characteristics of BC including stage.
- The blood Trx1 level could correct mis- or incompletely judged mammography with 93% efficiency. When mammography and Trx1 level were analyzed together, the accuracy was near 100%.

**Table 1.** Basic information of participating groups in this clinical trial

Group	Number	Age*	Group	Number	Age*
Breast cancer	308	54±11.2	Cervical cancer	40	49.4±11.6
Women without BC	254	59.1±9.39	Lung cancer	96	67.8±8.75
Benign Breast Disease	82	57.5±8.24	Stomach cancer	110	61.7±11.9
Ovarian cancer	33	51.9±11	Colorectal cancer	109	65.1±10

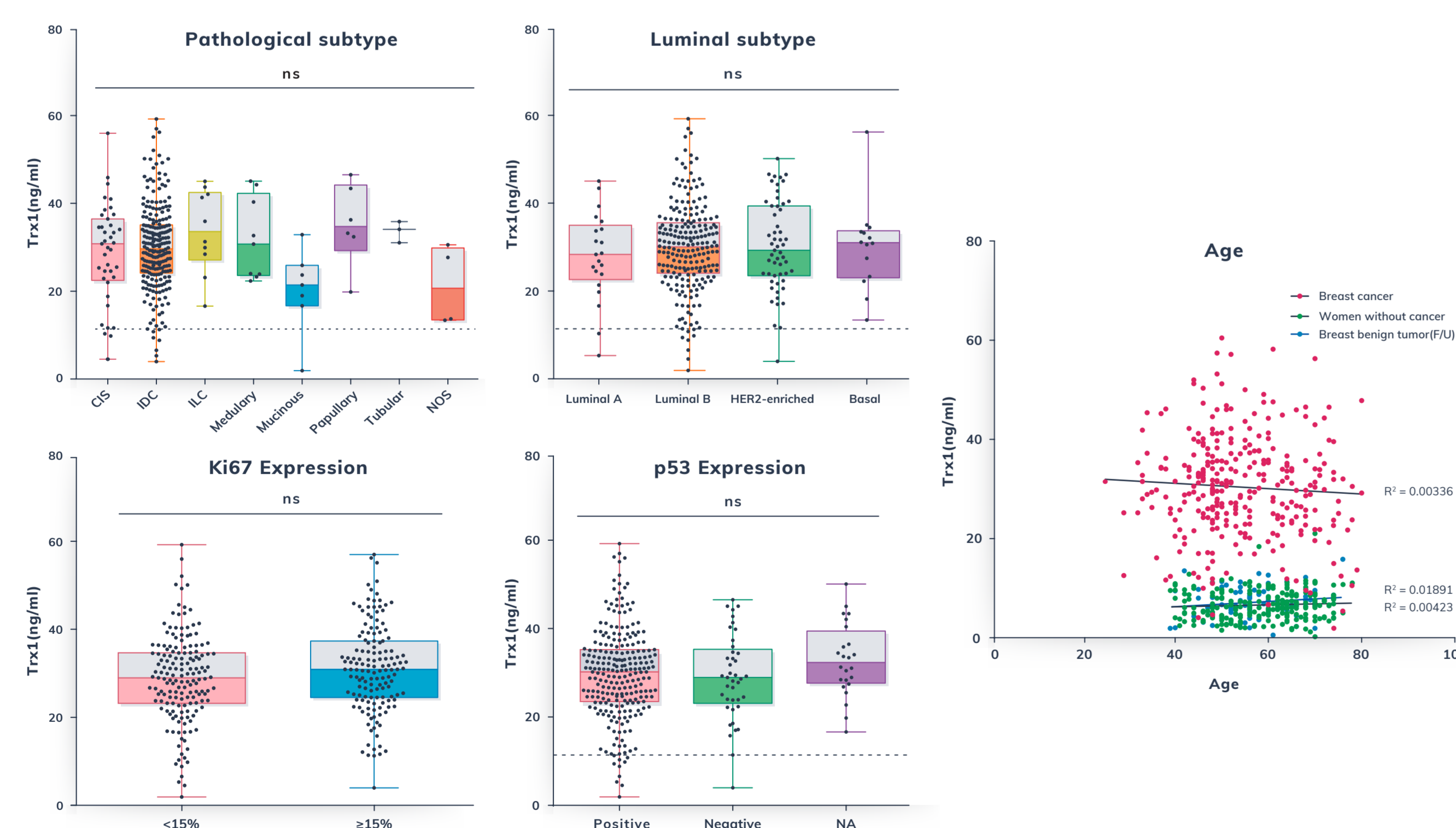
\* Age of each group indicates the average.

**FIG. 2.** Blood level of Trx1 from BC patients along with TNM stages



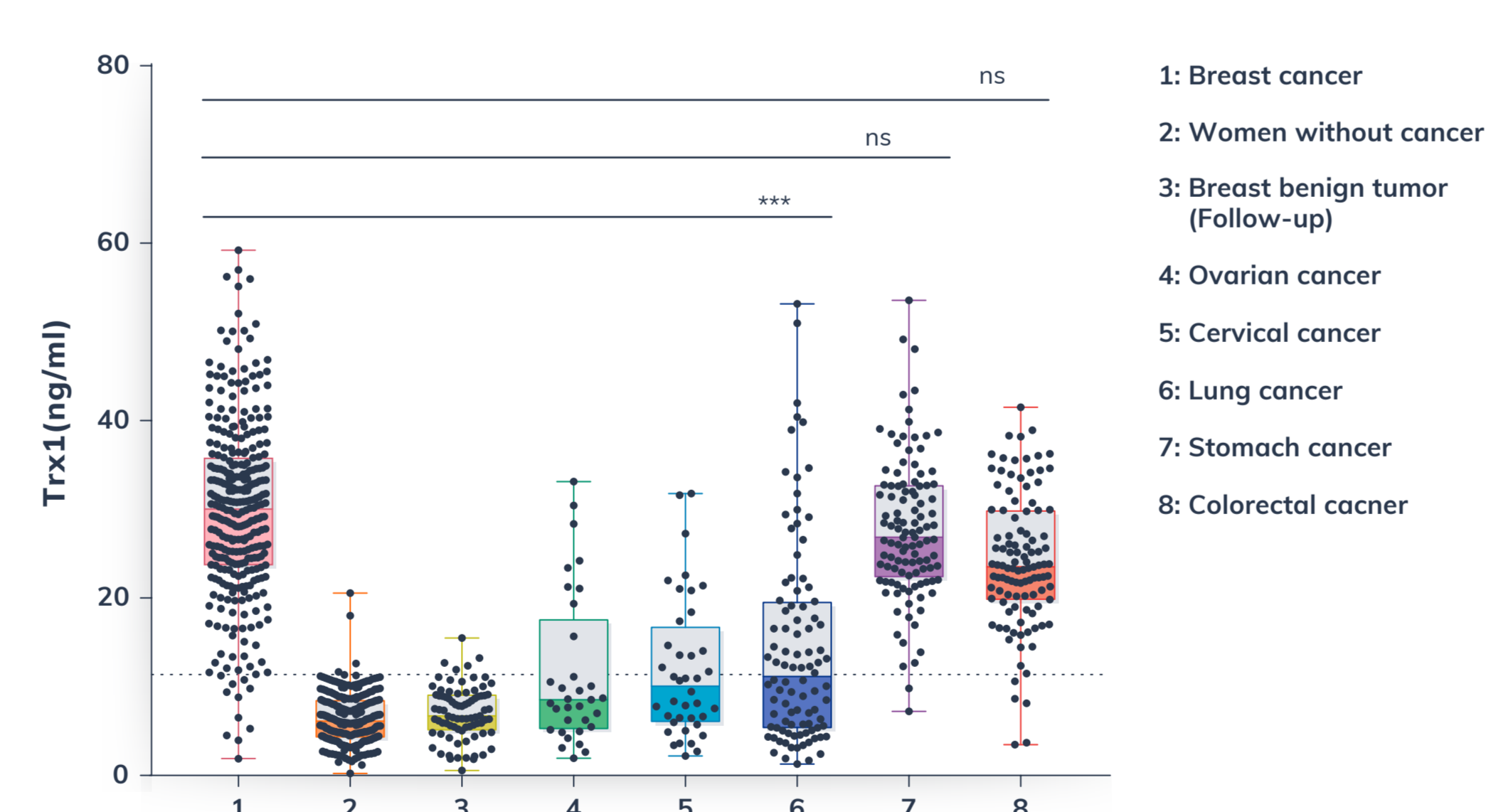
Biopsy-confirmed BC patients were grouped by BC characteristics, and the blood level of Trx1 was estimated. The level of Trx1 was analyzed according to the age of participants, pathological and luminal subtypes of BC, and expression profiles of Ki67 and p53. There was no correlation between Trx1 level and age of BC patients as well as control groups including breast benign tumor and women without cancer. The levels of blood Trx1 were remained much higher than the cut-off value (11.4 ng/ml) regardless of BC characteristics.

**FIG. 3.** The level of blood Trx1 according to physiological and pathological characteristics of BC



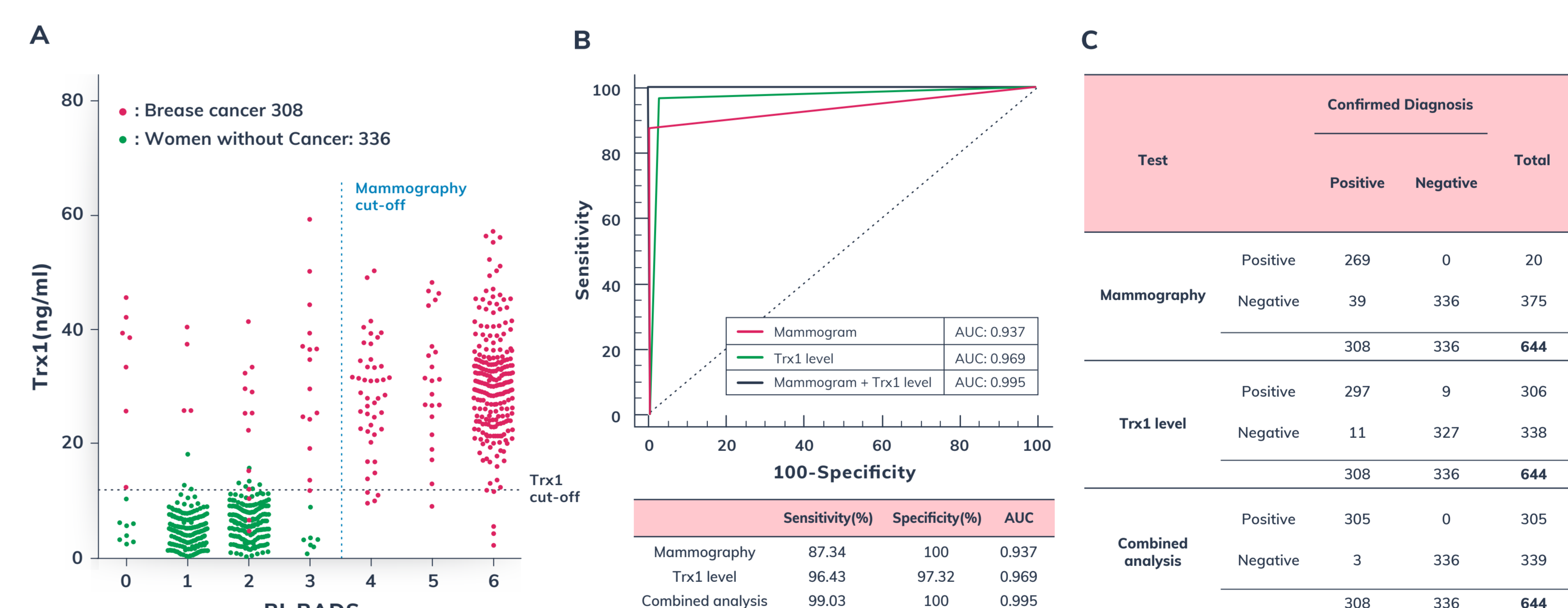
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**FIG. 4.** The level of blood Trx1 from BC and other types of cancer



The blood levels of Trx1 from BC and other types of cancer were estimated to see how Trx1 level can differentiate BC from other cancers. The blood Trx1 level in BC patients was much higher than those in breast benign tumor, women without cancer, ovarian cancer, cervical cancer, and lung cancer. There was no statistically significant difference among BC, stomach cancer, and colorectal cancer. 1; BC (n=308), 2; women without cancer (n=254), 3; breast benign tumor (n=82), 4; ovarian cancer (n=33), 5; cervical cancer (n=40), 6; lung cancer (n=96), 7; stomach cancer (n=110), 8; colorectal cancer (n=109).

**FIG. 5.** Complementary function of blood level of Trx1 to mammography



Previously obtained mammogram results of biopsy-confirmed BC patients were analyzed with the blood level of Trx1 from corresponding patients. (A) The results of mammography and Trx1 level estimations. The vertical dot line indicates the cut-off of mammography, and the horizontal dot line for that of Trx1 level test. Thirty-nine out of 308 confirmed BC patients were judged as false negative by mammography. Eleven cases were judged as false negative by blood level of Trx1. (B) ROC analysis of mammography, Trx1 level test, and combined test. If the result from one of the combined tests was positive, it was regarded as positive for patient's benefit. Concordance rate showing that positive results from one type of tests turned out to be true positive was higher than 91%. When mammography and Trx1 test combined to detect BC, its sensitivity and specificity were close to 100%. (C) Summary of comparative analysis of mammography with Trx1 level test.

**Conclusions:** Analyzing 1,032 blood samples, the level of blood Trx1 could discern BC regardless of its characteristics. It was also validated to be an effective detection tool to assist BC diagnosis in every stage. Thus, the blood level of Trx1 can be a novel aid to diagnose BC from blood.