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A whole blood assay to identify breast cancer: interim analysis of the international identify breast cancer (IDBC) study evidence supporting the Syantra DX | Breast Cancer test.

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Background: Breast cancer is often detected at later stages, indicating a significant need for additional screening methods. Mammography has limitations in breast cancer detection, for example young age, mammographic high density (categories C and D), small tumors and breast cancer classifications such as invasive lobular carcinomas. Syantra DX | Breast Cancer is a new whole blood test that detects the presence of breast cancer by evaluating the expression of 12 novel genes through a custom qPCR process with proprietary software that includes machine learning-derived algorithms.

Methodology: Whole blood samples (2.5 ml) were collected and analyzed with Syantra DX | Breast Cancer as part of the ongoing IDBC prospective international clinical study (NCT04495244). The study is designed to demonstrate test performance in 2,100 participants. Women aged 30 to 75 years with a normal screening mammogram or physical exam (for the controls), or a BI-RADs 3 – 5 score on a screening mammogram were enrolled. A total of 1,107 participants (240 asymptomatic breast cancer, 867 non-cancer) were recruited and evaluated. All blood samples were collected pre-biopsy. For this interim analysis, 383 samples (132 cancer, 251 non-cancer) were used for machine learning-based model development and initial testing using a cross-validation approach. A set of 724 samples, with 695 evaluable samples (blind test set: 96 cancer, 599 non-cancer) were used for independent testing. All samples in the test set were randomized and blinded by the Alberta Cancer Research Biobank. Clinical performance metrics are reported for the blind test set with 99.5% confidence intervals (CI) computed through an exact binomial test.

Results: In the blind test set, 59% of breast cancer subjects were Stage 1 and 25% stage 2. For molecular subtype, 75% were hormone receptor positive, 10% were HER2 positive, and 5% were triple negative. For subjects with invasive breast cancer, the average tumor size was 29 mm (CI: 19 – 38 mm). For the entire test set, Syantra DX | Breast Cancer demonstrated an inferred accuracy of 92.2% (CI: 88.9% – 94.6%) with a specificity of 94.3% (CI: 91.0% – 96.4%) and sensitivity of 79.2% (CI: 65.5% – 88.4%) for cancer detection (Table 1). Higher performance was observed in the group of study women under 50 with an inferred specificity of 99.0% and a sensitivity of 91.7% (Table 1). Evaluation of performance in women with extremely dense breast tissue (category D; n=52) revealed an inferred specificity of 95.3% (CI: 77.4% – 99.2%) and sensitivity of 88.9% (CI: 42.6% – 98.9%). This analysis also showed that small tumors less than 10 mm (n=19) were detected by the test, with a sensitivity of 68.4%.

Conclusions: Interim data from the IDBC study demonstrated the clinical utility of the Syantra DX | Breast Cancer test for use in early screening. Syantra DX | Breast Cancer is the first blood test to show strong performance for women under 50, as well for those with very high breast density, and therefore provides a promising screening option to supplement current imaging approaches.

Table 1: Performance Metrics of the Syantra DX | Breast Cancer test

| Age | Number of participants (n) | Accuracy | Specificity | Sensitivity |
|---------------|----------------------------|---------------------------|---------------------------|---------------------------|
| < 50 | Normal: 192 Cancer: 12 | 98.5% (CI: 93.8% – 99.7%) | 99.0% (CI: 94.2% – 99.8%) | 91.7% (CI: 51.1% – 99.1%) |
| ≥ 50 | Normal: 407 Cancer: 84 | 89.6% (CI: 85.1% – 92.9%) | 92.1% (CI: 87.5% – 95.1%) | 77.4% (CI: 62.5% – 87.5%) |
| Entire cohort | Normal: 599 Cancer: 96 | 92.2% (CI: 88.9% – 94.6%) | 94.3% (CI: 91.0% – 96.4%) | 79.2% (CI: 65.5% – 88.4%) |

See IDBC study on clinicaltrials.gov:

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About Syantra Inc.

Syantra Inc. is a precision healthcare company that's changing the way cancer detection and treatment are undertaken. Our flagship product, Syantra DX | Breast Cancer, is a blood-based, innovative method of detecting breast cancer.

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