# Risk stratification in early stage luminal breast cancer patients treated with and without RT

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## BACKGROUND

- The goal was to develop and validate a biologic signature for 10-year ipsilateral invasive breast event (IBE) risk in luminal Stage 1 breast cancer (BC) patients treated surgically, with or without adjuvant radiotherapy (RT).

## MATERIALS & METHODS

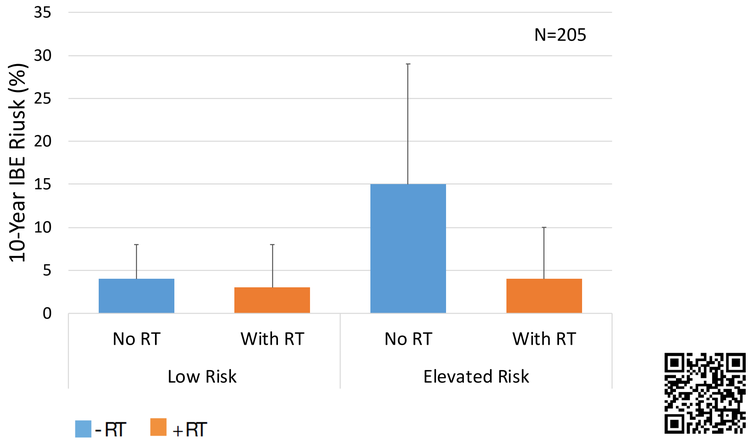
- This cohort was from Uppsala University and Västerås Hospitals diagnosed with Stage 1 BC and treated surgically between 1987 and 2004. Treatment was neither randomized nor strictly rules based, including adjuvant RT, hormone therapy (HT), and chemotherapy (CT).
- Biomarkers (HER2, PR, Ki67, COX2, p16/INK4A, FOXA1 and SIAH2) were assessed on tissue microarrays in PreludeDx's CLIA lab by board-certified pathologists. Risk groups were calculated using biomarkers and the clinical factors age and size. A multivariate Cox proportional hazards analysis was used to determine hazard ratio for biologic signature. The 10-year IBE risk was assessed using Kaplan-Meier survival analysis.

## RESULTS

- There were 423 luminal cases with biomarker data having 54 IBEs, during a median follow-up of 11.8 years. There were 372 patients treated with BCS and 51 with mastectomy, and 325 received RT, 169 received HT, and 47 received CT. In a multivariate analysis, the biologic signature (HR = 1.6, p = 0.019) and RT (HR = 0.51, p = 0.027) were associated with IBE risk adjusting for other treatments (HT and CT) and Luminal A status (p = 0.37). Luminal A* status was defined as PR neg (<1%), KI67 neg (< 15%) and HER2 neg (<3)
- For patients over 50 years of age with luminal A disease and treated without CT (n = 205), the biologic signature identified a subset of patients with an elevated risk; 15% (+/- 14%) 10-year IBE risk without RT (n = 38) compared to a 4% (+/-6%) IBE risk with RT (n = 72), while patients with a low biologic signature risk had a 10-year IBE risk of 4% (+/- 4%) without RT (n = 26) and 3% (+/-5%) IBE risk with RT (n = 69).

- **The biologic risk signature identifies subgroups of patients with early-stage BC who will benefit from RT**
- **In Luminal A* breast cancer, the signature provides both prognostic and predictive value for RT benefit**

## 10-YEAR IBE RISK




## DISCUSSION

- A biological risk signature based on 7 biomarkers and clinic-pathological factors identified a group of patients with invasive Luminal A breast cancer with a 10-year risk of 15% for local recurrence, and a substantial benefit from RT. A low risk group with a 4% risk of local recurrence at 10 years was also identified, with a minimal absolute benefit from RT.
- With further prospective validation, the biologic signature identified herein may provide a tool enabling improved management for women diagnosed with early luminal breast cancer.

## TABLE 1 – POPULATION CHARACTERISTICS

| ALL LUMINAL CASES (n=423) | - RT (%) | + RT (%) | (N) |
|---|---|---|---|
| **Age Group** | | | |
| <=50 years | 8 | 92 | 112 |
| >50 years | 29 | 71 | 311 |
| **Tumor Size Group** | | | |
| <= 10 mm | 29 | 71 | 205 |
| >=10 mm | 17 | 83 | 218 |
| **Nuclear Grade** | | | |
| Grade 1 & 2 | 24 | 76 | 389 |
| Grade 3 | 9 | 91 | 33 |
| **CT** | | | |
| No | 26 | 74 | 376 |
| Yes | 2 | 98 | 47 |
| **Luminal A** | | | |
| No | 20 | 80 | 137 |
| Yes | 25 | 75 | 286 |
| **HT** | | | |
| No | 28 | 72 | 254 |
| Yes | 17 | 83 | 169 |

## TABLE 2 – MULTIVARIATE ANALYSIS

| 10-YEAR IBE RISK (n=423, 54 events) | IBE | | |
|---|---|---|---|
| | **HR** | **[95 %, CI]** | **P-Value** |
| **RT** | 0.51 | [0.28 - 0.93] | 0.03 |
| **Biosignature** | 1.58 | [1.08 - 2.32] | 0.02 |
| **Luminal A** | 0.77 | [0.43 - 1.37] | 0.37 |
| **CT** | 0.71 | [0.25 - 2.04] | 0.52 |
| **HT** | 0.75 | [0.46 - 1.24] | 0.26 |
| **Mastectomy** | 0.60 | [0.23 - 1.53] | 0.28 |

## TABLE 3 – 10-YEAR IPSILATERAL INVASIVE BREAST EVENT (IBE) RISK TREATED SURGICALLY AND EITHER WITH OR WITHOUT RADIATION THERAPY (RT) (n=205)

| | BCS – RT | | | BCS + RT | | |
|---|---|---|---|---|---|---|
| | **Risk [95%, CI]** | **Prevalence** | **(N)** | **Risk [95%, CI]** | **Prevalence** | **(N)** |
| **Low Risk** | [0.88 – 1.0] | 4% (+/- 4%) | 26 | [0.93 – 1.0] | 3% (+/-5%) | 69 |
| **Elevated Risk** | [0.73 – 1.0] | 15% (+/- 14%) | 38 | [0.91 – 1.0] | 4% (+/-6%) | 72 |