Outcome of patients with an ultralow risk 70-gene signature in the MINDACT trial

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Increase in the incidence and survival of breast cancer

Figure: Trends in Breast Cancer Incidence by Stage in Women over 50 in the Netherlands, 1989-2012

Gene signatures can identify patients at low risk of distant recurrence

- 70-gene signature
- Level 1 clinical utility
- Preserved outcome without chemotherapy

70-gene signature Low and Ultralow risk tumors overrepresented in screen-detected cancers

Ultralow risk patients have excellent survival in historic cohorts

Validation cohorts:
- 98% no AST
- 15-year BCSS 100%

STO-3, 1976-1990
LNO, <3cm, 339 received tamoxifen, 313 received no AST
20-year BCCS for ultralow risk patients:
- 97% for patients receiving tamoxifen
- 94% for patients receiving no AST

Assess survival outcome of MINDACT patients with an ultralow risk tumor biology

Can the identification of patients with an ultralow risk 70-gene signature help to avoid overtreatment in early-stage breast cancer?
Inclusion criteria

- Women aged 18-70
- Operable invasive breast cancer
- Tumor size max 5 cm
- 0-3 positive lymph nodes
- No distant metastasis


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15% of MINDACT patients genomic ultralow risk

- **HR+/HER2- subtype**
  - ~95% of Low* and Ultralow risk patients
  - 57% of High risk patients

- **Adjuvant systemic treatment**
  - 76-85% endocrine therapy or no AST in Low and Ultralow risk
  - 83% chemotherapy in High risk

*Low risk also referred to as Low not Ultralow

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**70-gene signature result**

- **Ultralow risk**
  - 1000
  - 15%
  
- **Low risk**
  - 2398
  - 36%

- **High risk**
  - 3295
  - 49%

Total N=6693
Excellent Distant Metastasis Free Interval rates for genomic Low and Ultralow risk patients

Median follow-up: 8.7 years

<table>
<thead>
<tr>
<th>Risk of distant metastasis or BC-death</th>
<th>Adj* HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultralow risk vs low risk</td>
<td>0.65 (0.45-0.94)</td>
</tr>
<tr>
<td>High risk vs low risk</td>
<td>2.17 (1.68-2.80)</td>
</tr>
</tbody>
</table>

*Adjusted for clinical-pathological and treatment characteristics
Excellent Breast Cancer Specific Survival rates for genomic Low and Ultralow risk patients

- **Events**: 8
- **8-year BCSS**: 99.6% (99.1-100)
- **Events**: 69
- **8-year BCSS**: 98.2% (97.7-98.7)
- **Events**: 160
- **8-year BCSS**: 93.7% (92.6-94.7)
Characteristics 1000 genomic Ultralow risk patients

- 67% >50 years
- 80% lymph node negative
- 81% tumors ≤2 cm
- 96% Grade 1 or 2
- 97% HR+/HER2- subtype
- 16% no adjuvant systemic treatment
- 69% endocrine therapy
- 14% chemotherapy

Clinical risk

- Low risk: 741
- High risk: 259

Clinical High risk tumors
- Larger size
- Higher grade
- Lymph node positive
Small difference in Distant Metastasis Free Interval in genomic Ultralow risk patients by Clinical risk

Events 8-year DMFI

- Clinical Low risk: 21, 97.6% (96.4-98.8)
- Clinical High risk: 15, 95.0% (92.3-97.8)
No difference in Breast Cancer Specific Survival in genomic Ultralow risk patients by Clinical risk

Events 8-year BCSS

Clinical Low risk 6 99.7% (99.3-100)
Clinical High risk 2 99.2% (98.0-100)
Excellent outcomes for genomic Ultralow risk patients receiving only endocrine therapy or no adjuvant systemic treatment.

Risk of distant metastasis or BC-death (Ultralow risk patients only)

<table>
<thead>
<tr>
<th>Treatment received</th>
<th>Events</th>
<th>8-year DMFI</th>
</tr>
</thead>
<tbody>
<tr>
<td>No AST (n=157)</td>
<td>4</td>
<td>97.8% (95.3-100)</td>
</tr>
<tr>
<td>ET only (n=685)</td>
<td>23</td>
<td>97.4% (96.1-98.7)</td>
</tr>
<tr>
<td>CT +/- ET (n=144)</td>
<td>8</td>
<td>94.9% (94.4-98.7)</td>
</tr>
</tbody>
</table>

CT vs no CT: 0.98 (0.37-2.61)
ET vs no ET: 0.59 (0.27-2.13)

*Adjusted for clinical-pathological characteristics

Note: 92% of patients receiving chemotherapy were Clinical High risk
Conclusions

- 70-gene signature ultralow risk patients have excellent 8-year DMFI and BCSS

- Very few patients developed distant metastases

- Excellent DMFI rates for patients who received only endocrine therapy or no adjuvant systemic treatment

- Confirmation of previously published results in the largest cohort of ultralow risk patients to date

Clinical implications

- The 70-gene signature MammaPrint can identify patients with an ultralow risk of distant recurrence

- Patients with ultralow risk tumors could be candidates for further de-escalation of treatment, further reducing overtreatment and the risk of side-effects
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Questions?

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