An exploratory comparison of MINDACT and TAILORx genomic risk proportions and outcomes in patients with HR+/HER2-, node-negative early-stage breast cancer, stratified by clinical risk

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Background

- Genomic tests provide physicians with critical information to evaluate the risk of distant metastasis and inform treatment plans by identifying those patients with early-stage breast cancer who may safely avoid chemotherapy (CT)
- The 70-gene signature (MammaPrint®, MP) through the MINDACT trial[1] and the 21-gene signature (Oncotype DX®, ODX) through the TAILORx trial[2,3] are the only tests validated with level 1A evidence that can be used for CT de-escalation decisions
- In MINDACT, all patients in the randomized groups were clinical high risk, versus 26% in TAILORxHere, we identified the comparable populations in both MINDACT and TAILORx trials

Are proportions of patients with genomic low risk comparable between MammaPrint and Oncotype DX?

Methods

Data included:

- Data for patients with HR+/HER2- N0 disease from the MINDACT (n = 4425) and TAILORx (n = 9719, prior adjustment) publications were included[1,2,3]. Publicly available data on the original TAILORx population from the Dutch Health Technology Assessment authorities were also included[4]
- Patients are reported as genomic low risk with a MammaPrint Low Risk in MINDACT or an ODX Low (Recurrence Score [RS] 0–10) or ODX Intermediate (RS 11–25) in TAILORx
- In MINDACT, randomization was based on both clinical and genomic risk. In TAILORx, randomization was based on genomic risk alone, though later analyzed using clinical risk stratification (per MINDACT definition)

MammaPrint and Oncotype DX show comparable proportions of patients with genomic low risk in the MINDACT and TAILORx trials

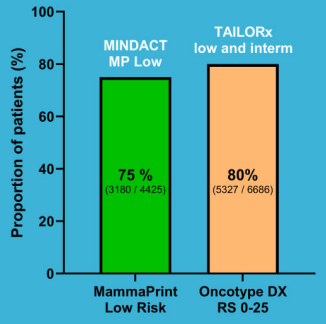

Figure 1. All HR+/HER2- N0 patients: MammaPrint and Oncotype DX genomic risk distribution in MINDACT and TAILORx

Interm. Intermediate; MP. MammaPrint; ODX RS. Oncotype DX Recurrence Score.

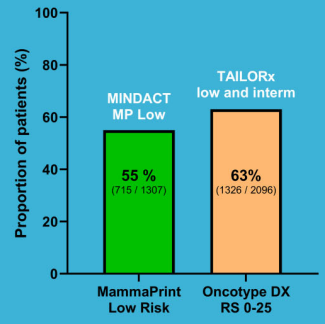

Figure 2. Clinical High Risk HR+/HER2- N0 patients: MammaPrint and Oncotype DX genomic risk distribution in MINDACT and TAILORx

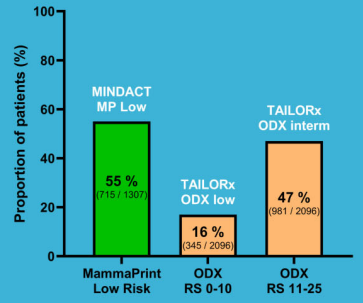

Figure 3. Clinical high risk HR+/HER2- N0 patients: MammaPrint and Oncotype DX genomic risk distribution in MINDACT and TAILORx.

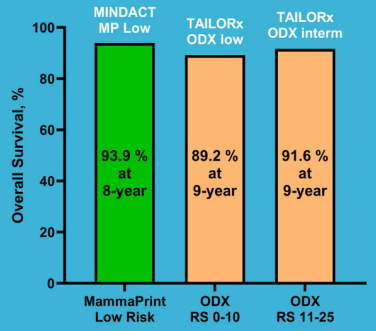

Figure 4. Overall survival in patients with clinical high risk and genomic low risk in MINDACT (A, MammaPrint Low Risk at 8-year) and TAILORx (B, Oncotype DX RS 0–10, and C. ODX RS 11–25, at 9-year) **not treated with chemotherapy**

OS data presented per original MINDACT and TAILORx populations. Figures adapted from Piccart et al.[1] for MINDACT, and Dutch HTA report for TAILORx[4].

Methods (continued)

Trials description:

Extrapolated population of the RS 11–25 group in TAILORx:

- Enrollment in the RS 11–25 group was extended by 73%, per amended protocol, almost doubling the size of this group in the trial to account for the initially observed non-treatment adherence in the randomization, as described in the original publication[2]
- For the purpose of this comparison of proportion of patients with genomic low risk in MINDACT and TAILORx, the enrollment extension was removed by applying a proportional 73% reduction to the RS 11–25 group (ie. dividing patient number by 1.73), resulting in a total of 6686 patients considered from TAILORx, among those 1572, 3755 and 1359 with RS 0-10, RS 11–25 and RS>25, respectively. When stratifying by clinical risk, it was estimated that 2096 patients had clinical high risk tumors
- Data presented in Figure 1 – 3 are based on the adjusted TAILORx population

Results

Genomic risk distributions in MINDACT (MammaPrint Low) and TAILORx (ODX RS 0–10 & adjusted ODX RS 11–25 group):

- Similar proportions of patients identified as candidates for CT de-escalation (MammaPrint Low Risk or ODX RS 0–25) were observed in MINDACT (75%) and TAILORx (80%) when removing the ODX RS 11–25 population extension in TAILORx (**Figure 1**)
- In clinical high risk patients, the proportion with genomic low risk were also comparable between MINDACT (55% MammaPrint Low Risk) and TAILORx (63% ODX RS 0–25) (**Figure 2 and 3**). In TAILORx, this proportion could be further divided into 16% ODX Low RS 0–10, and 47% ODX Intermediate RS 11–25

Long-term outcomes in clinical high risk and genomic low risk patients in the original trials

- In MINDACT patients with clinical high risk but MammaPrint Low Risk treated without CT had an 8-year OS of 93.9% (**Figure 4**)
- In TAILORx, the comparable population of patients with clinical high risk, low genomic risk, not treated with CT had a 9-year OS of 89.2% in the RS 0–10 group and 91.6% in the RS 11–25 group (**Figure 4**)

Conclusions

- Accounting for differences in trial design and population, comparable proportions of patients with breast cancer with genomic low risk results were observed between MammaPrint and Oncotype DX in both the overall trial population and the clinical high risk population, justifying similar rates of CT de-escalation
- Patients with clinical high risk tumors who are MammaPrint Low Risk had an excellent survival at 8 years

References – 1. Piccart et al. Lancet Oncol. 2021. 22(4):476-488. 2. Sparano et al. N Engl J Med. 2018. 379:111-121. 3. Sparano et al. N Engl J Med. 2019. 380:2395-2405. 4. Standpunt Oncotype bij vroeg stadium borstkanker. Zorginstituut Nederland. bit.ly/40eWnKq. Accessed 31 Oct 2023.

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