Should genomic risk guide the use of adjuvant CDK4/6i in N0-N1 HR+/HER2− early breast cancer?

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Background

Multigene prognostic genomic assays (MPGA) have enabled improved selection of patients who are likely to benefit from chemotherapy (CT) in adjuvant setting of HR+/HER2− breast cancer. Moreover, the addition of CDK4-6 inhibitors (CDK4-6i) to endocrine therapy (ET) has demonstrated a significant improvement iDFS in high risk (HR) patients (1,2). However, there is currently no standardized definition of high clinical risk, and correlation between clinicopathological features and genomic risk subgroups (GRS) is not consistently observed (3). This lack of concordance introduces uncertainty regarding the clinical benefit of adding CDK4-6i to ET in this setting (4).

Objetives

The aim of this study is to describe a population of patients with early-stage (N0-N1) HR+/HER2- breast cancer who underwent MPGA (either Prosigna® or Oncotype DX®) and met the inclusion criteria of the NATALEE trial, with the aim of determining whether the addition of a CDK4-6i to ET provides a clinical benefit in this setting.

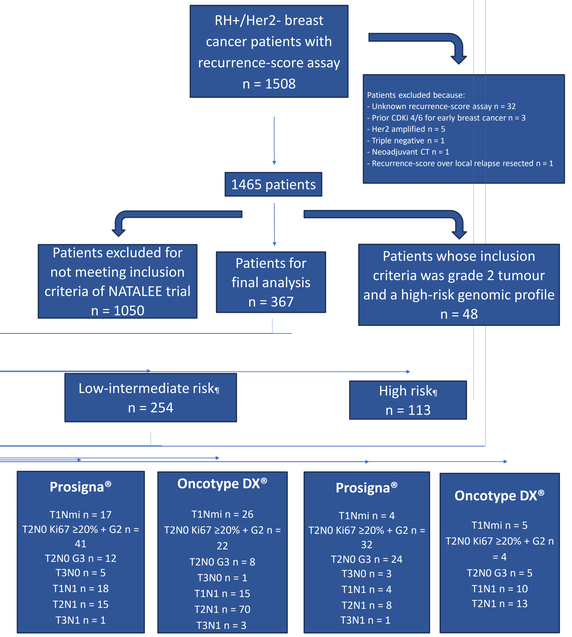
Methods and Materials

This retrospective study included patients diagnosed with early-stage (N0-N1) HR+/HER2- breast cancer between 2014 and 2023 across two hospitals in Malaga, Spain (Hospital Virgen de la Victoria and Hospital Regional Universitario). Efficacy outcomes were iDFS, DDFS and OS. The statistical analysis was performed using the R software.

Results

Median age was 61 years (29-82). Most of them were premenopausal (72,8%), and 1,1% were men. The main clinicopathological characteristics are summarized in Table 1. 46.3% of patients received CT, predominantly among patients with high genomic risk. With a median follow-up of 37.4 months, there were 30 iDFS events (8,2%). The 3-year iDFS rate was 94.9% (95% CI, 92% to 96.8%) in the overall population, 94.8% (95% CI, 91.1% to 97.1%) in the low/intermediate (L/I) GRS, 95.2% (95% CI 88.8% to 98%) in the high GRS, 94.3% (95% CI 90.8% to 96.5%) in stage II, 94.1% in N0 (95% CI, 89% to 97%), and 95.6% (95% CI, 91.2% to 97.7%) in N1 disease. DDFS and OS events occurred in 11 (2.9%) and 12 patients (3.26%) respectively. 3-year OS rates were 98.7% (95% CI 96,7% to 99.5%) in the overall population, 98.2% (95% CI 95.3% to 99.3%) in the L/I GRS and 98.6% (95% CI 90.4% to 99.8%) in the HR GRS.

Figure 1. Flow chart of the patient population



¶ Risk by Prosigna® was determined by ROR (risk of recurrence): low 0-40; intermediate 41-60; high 61-100. Risk by Oncotype DX® was determined by RS (recurrence score): low 0-25; high 26-100

Table 1. Demographic and baseline clinical characteristics

Characteristic	Patients (n=367)
Anatomical stage - no. (%)†	
IB	52 (14,2)
IIA	195 (53,1)
IIB	115 (31,3)
III	5 (1,4)
Nodal status at surgery - no. (%)‡	
NX	0 (0)
N0	157 (44,6)
N1mi	53 (14,4)
N1	157 (44,6)
Histologic grade at diagnosis - no. (%)	
1	37 (10,1)
2	232 (63,2)
3	98 (26,7)
Adjuvant endocrine therapy - no. (%)	
Ovarian function–suppression therapy	17 (4,6)
Aromatase inhibitor	258 (70,5)
Antiestrogen	89 (24,2)
Other	2 (0,6)
None	2 (0,6)

Characteristic	Patients (n=367)
Previous neoadjuvant/adjuvant CT - no. (%)	
Any	170 (46,3)
Taxanes	65 (17,7)
Anthracyclines	42 (11,4)
Both	63 (17,2)
Neoadjuvant	0 (0)
Adjuvant	36 (99,7)
Previous neoadjuvant/adjuvant CT - no. (%)	
Any	170 (46,3)
Taxanes	65 (17,7)
Anthracyclines	42 (11,4)
Both	63 (17,2)
Neoadjuvant	0 (0)
Adjuvant	36 (99,7)
Inmunochemistry subtype - no. (%) §	
Luminal A	91 (25,1)
Luminal B	275 (74,9)
Intrinsic subtype by Prosigna® - no. (%)	185
Luminal A	76 (40,7)
Luminal B	104 (56,2)
Her2 enriched	5 (2,7)

Characteristic	Patients (n=367)
Adjuvant CT based on genomic risk – no. (%)	
Prosigna®	108
Low	8 (17,7)
Intermediate	35 (54,7)
High	65 (85,6)
Oncotype DX®	62
Low	26 (17,9)
High	36 (97,3)
Histologic type - no. (%)	
Invasive ductal not otherwise specified	296 (80,7)
Invasive lobular	50 (13,6)
Ducto-lobular	8 (2,2)
Mucinous	4 (1,1)
Papillary	6 (1,6)
Other	(0,8)
Genomic Platform - no. (%) ¶	
Prosigna®	185 (50,4)
Low	45 (12,3)
Intermediate	64 (17,4)
High	76 (20,7)
Oncotype DX®	182 (49,6)
Low	145 (39,5)
High	37 (10,1)

† The stage was derived with the use of tumour–node–metastasis (TNM) staging that was determined at the time of surgery.
‡ N0 indicates no nodal involvement, N1 indicates 1 to 3 axillary lymph nodes, N2 indicates 4 to 9 axillary lymph nodes and NX indicates that regional lymph nodes were not assessed. Nodal status was evaluated according to the American Joint Committee on Cancer Staging Manual, Eighth Edition.
§ Immunochemistry subtype was determined by Ki67 cut-off: <14% was luminal A and ≥15% was luminal B.
¶ Prosigna® risk was determined by ROR (risk of recurrence): low 0-40; intermediate 41-60; high 61-100. Risk by Oncotype DX® was determined by RS (recurrence score): low 0-25; high 26-100

Conclusions

The findings suggest that the use of adjuvant CDK4-6i in N0 or N1 HR+/HER2− breast cancer should be guided by MPGAs results in L/I and high-risk patients. Prospective studies are needed to better validate this hypothesis.

Contact

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