Real-World Evidence from FLEX: Utility of MammaPrint® in guiding treatment planning for patients aged 70 and older with early-stage breast cancer

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Background

- Older women (≥70) are less likely to receive chemotherapy (CT) due to quality-of-life concerns[1,2]
- Older patients are underrepresented in studies assessing the utility of genomic profiling in guiding CT decisions[1,2]

- **Objective:** To examine the relationship of age (≥70 vs.<70) and treatment outcomes stratified by MammaPrint subtypes in pts with HR+HER2- early-stage breast cancer (EBC) to identify the utility of MammaPrint in informing treatment decisions

Methods

Study Cohort

- Patients with HR+HER2- EBC (N=4619) enrolled in the ongoing prospective, observational FLEX Trial (NCT03053193) who received MP with or without BP testing with outcomes data available were included in this study.
- Pts were stratified into age groups < 70 years (N=3472) and ≥ 70 yr (N=1047).

MammaPrint Testing Results:

Statistics

- Differences in the distribution of clinical characteristics between age groups were assessed by Chi-squared, Fisher's exact, or Wilcoxon-Mann-Whitney tests.
- The endpoint recurrence-free interval (RFI)[3] was defined as time to local, regional, or distant recurrence or breast cancer related death Kaplan-Meier survival analysis and log-rank tests were used to assess differences in endpoints between treatment groups.

References

1. Hutchins et al., N Engl J Med, 1999; 2. Lacaze et al., Cancers, 2021; 3. Tolaney et al., JCO, 2024

Table and Figures

Table 1. Clinical Characteristics

Variable		Total N=4519 (%)	< 70 yr N=3472 (%)	≥ 70 yr N=1047	P-value
Menopausal status	Pre-/Peri-	897 (21.1)	896 (27.7)	1 (0.1)	<0.001
	Post-	3363 (78.9)	2343(72.3)	1020 (99.9)	
Grade	G1	1392 (31)	1067 (30.9)	325 (31.2)	0.022
	G2	2412 (53.6)	1827 (52.9)	585 (56.1)	
	G3	692 (15.4)	559 (16.2)	133 (12.8)	
Tumor Stage	T1	2696 (66.7)	2252 (65.8)	717 (69.5)	0.107
	T2	1264 (28.4)	989 (28.9)	275 (26.6)	
	T3	190 (4.3)	156 (4.6)	34 (3.3)	
	T4	29 (0.7)	23 (0.7)	6 (0.6)	
Lymph Node Status	LN-	3390 (76.6)	2584 (75.8)	806 (79.4)	0.017
	LN+	1034 (23.4)	825 (24.2)	209 (20.6)	
MammaPrint	UltraLow	673 (14.9)	519 (14.9)	154 (14.7)	0.048
	Low	1775 (39.3)	1344 (38.7)	431 (41.2)	
	High1	1671 (37)	1280 (36.9)	391 (37.3)	
	High2	400 (8.9)	329 (9.5)	71 (6.8)	

Figure 1. CT treated patients stratified by age group and MP risk g

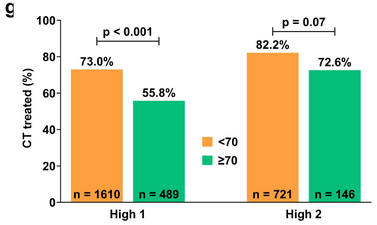
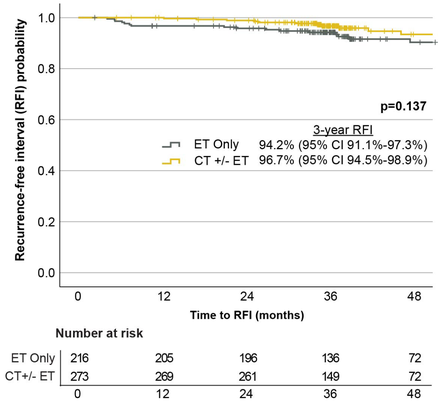
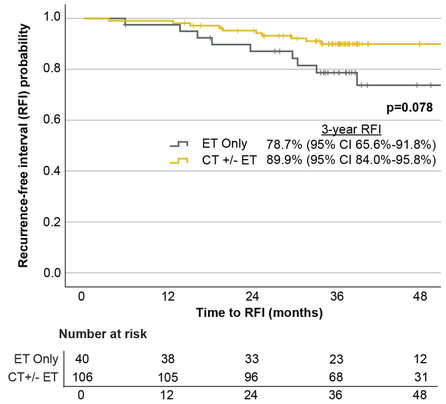


Figure 2. Recurrence Free Interval for pts ≥ 70 yr stratified by CT vs No CT

a. MP High 1



b. MP High 2



Results

- Patients ≥70 were significantly less likely to present with high grade tumors and lymph node involvement than those <70 (12.8% vs 16.2% grade 3, p=.022; 20.6% vs 24.2% node positive, p=.017, respectively) **(Table 1).**
- The MP risk group distribution showed a significantly higher proportion of low genomic risk (Ultralow or low risk) tumors in the ≥70 vs. <70 group (Ultralow (UL) 14.7% vs 14.9% , Low 41.2% vs 38.7% , High 1 (H1) 37.3% vs 36.9% , and High 2 (H2) 6.8% vs 9.5% , p 0.048, respectively) **(Table 1).**
- Patients ≥70 with MP High Risk (H1 or H2) tumors were less likely to receive CT compared to those <70 (H1 55.8% vs 73%, p<0.001; H2 72.6% vs 82.2%, p=0.07, respectively) **(Figure 1).**
- When evaluating 3-year RFI, the ≥70 pts with MP High Risk cancer trended towards better outcomes with CT than those receiving endocrine therapy only, especially in H2 cancers (H1 97% vs 94% , p=.137, H2 90% vs 79% , p=.078, respectively) **(Figure 2)**.

Conclusions & Future Directions

- This study underscores the potential CT benefits in MP H2 HR+ HER2- EBC pts ≥ 70 who may forgo treatment due to overall health and quality of life concerns.
- Notably, in MP H2 pts, the absolute improvement in 3-year RFI of 11% with neo/adjuvant CT in women ≥ 70 suggests that for selected pts, the benefit outweighs the risks.
- Of note, this H2 CT benefit is similar to that observed in a group of 1000 pts with a median age of 59 recently reported (Brufsky, et al. SABCS 2024, P2-08-12).
- Patient centered discussions on performance status, comorbidities, and genomic profiling of HR+ HER2- EBC as well as the potential benefit from CT should guide personalized treatment.