Improved 3-year IDFS with anthracycline-based therapy for patients with 70-gene signature High 2, Luminal B, HR+HER2- early-stage breast cancer

Joyce O'Shaughnessy[1], Adam Brufsky[2], Cathy Lynne Graham[3], Cynthia R. C. Osborne[4], Rakhshanda Layeequr Rahman[5], Ahmed Elkhanany[6], Eric Allen Brown[7], Linsey P. Gold[7], Nathalie M. Johnson[8], Danilo Giffoni[9], J. Jaime Alberty-Oller[10], Reshma L. Mahtani[11], Harshini Ramaswamy[12], Nicole Stivers[12], Andrea R. Menicucci[12], William Audeh[12], FLEX Investigators' Group

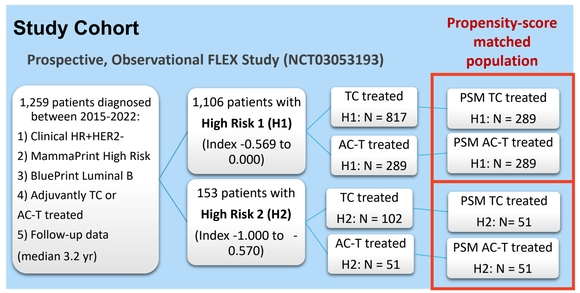
[1]Baylor University Medical Center, Texas Oncology, Sarah Cannon Research Institute, Dallas, TX; [2]University of Pittsburgh, Pittsburgh, PA; [3]Piedmont Cartersville Breast, Carterville, GA; [4]Texas Oncology, Dallas, TX; [5]Texas Tech University Health Sciences Center School of Medicine, Lubbock, TX; [6]Baylor College of Medicine, Houston, Texas; [7]Comprehensive Breast Care, Troy, MI; [8]Legacy Health System, Portland, OR; [9]London Regional Cancer Program, London, Ontario, CA; [10]Kings County Hospital Center, Brooklyn, NY; [11]Miami Cancer Institute, Baptist Health South Florida, Miami, FL;[12]Medical Affairs, Agendia, Inc., Irvine, CA

San Antonio Breast Cancer Symposium®
Presentation ID: PS2-07-03, Date: Dec 10, 2025

Introduction

- ABC trials[1] found no significant differences in outcomes among patients with clinically high-risk HR+, HER2- breast cancer when comparing adjuvant therapy with taxane+cyclophosphamide (TC) vs. an anthracycline- and taxane-based regimen (TaxAC)
- The MammaPrint®, 70-gene assay, identifies patients who derive (neo)adjuvant chemotherapy benefit[2] and the BluePrint, 80-gene assay, further classifies genomic molecular cancer subtype
- Here we provide an updated analysis[3] within a propensity score matched population (PSM) examining the utility of MammaPrint in identifying patients with BluePrint Luminal B, HR+HER2- breast cancer likely to benefit from anthracycline+taxane (AC-T) vs. TC

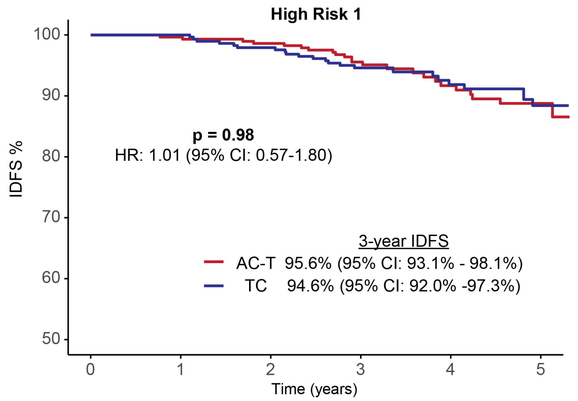
Methods



Statistics

- PSM was performed to balance differences in age, tumor size and nodal status between the TC and AC-T -treated pts for the H1 and H2 groups, separately.
- 3-yr invasive disease-free survival (IDFS)[4], was compared within H1 and H2 groups using Kaplan-Meier analysis and log-rank tests, stratified by TC vs. AC-T
- Cox proportional hazards models were used to evaluate the effect of CT regimen and clinical features on survival within each group

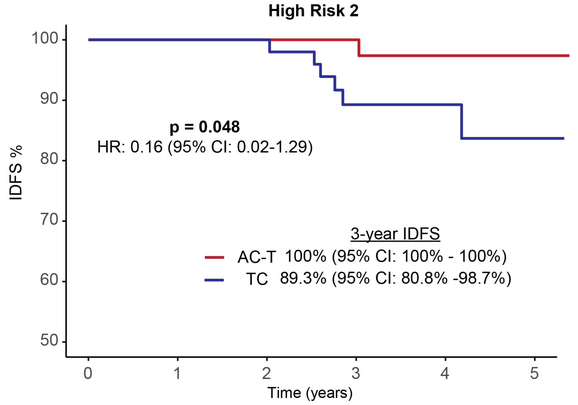
Figure 1. IDFS in patients with High Risk 1 cancer: AC-T vs. TC



Numbers at Risk

H1	0	1	2	3	4	5
AC–T	289	286	277	210	129	59
TC	289	288	276	207	132	70

Figure 2. IDFS in patients with High Risk 2 cancer: AC-T vs TC



Numbers at Risk

H2	0	1	2	3	4	5
AC–T	51	50	49	40	17	8
TC	51	51	50	30	16	9

Tables 1-2. Clinical Characteristics of FLEX patients with HR+HER2- disease PSM between AC-T or TC treatment in High Risk 1 (left) and High Risk 2 (right)

High Risk 1	AC-T (N=289)	TC (N=289)	Overall (N=578)	P-value
Age (Years)				
Mean (SD)	54 (± 11)	54 (± 11)	54 (± 11)	0.955
Menopausal Status				
Pre-/Peri-	94 (32.5%)	97 (33.6%)	191 (33.0%)	0.97
Post-	170 (58.8%)	163 (56.4%)	333 (57.6%)	
Unknown	25 (8.7%)	29 (10.0%)	54 (9.3%)	
Race/Ethnicity				
AAPI	10 (3.5%)	15 (5.2%)	25 (4.3%)	0.965
AIAN	1 (0.3%)	0 (0%)	1 (0.2%)	
Black	35 (12.1%)	29 (10.0%)	64 (11.1%)	
Latin American/Hispanic	21 (7.3%)	13 (4.5%)	34 (5.9%)	
Multiple	1 (0.3%)	1 (0.3%)	2 (0.3%)	
White	203 (70.2%)	210 (72.7%)	413 (71.5%)	
Unknown	18 (6.2%)	21 (7.3%)	39 (6.7%)	
Tumor Size				
T1	146 (50.5%)	144 (49.8%)	290 (50.2%)	0.99
T2	125 (43.3%)	131 (45.3%)	256 (44.3%)	
T3	15 (5.2%)	10 (3.5%)	25 (4.3%)	
T4	1 (0.3%)	1 (0.3%)	2 (0.3%)	
Unknown	2 (0.7%)	3 (1.0%)	5 (0.9%)	
Lymph Node Status				
LN-	159 (55.0%)	182 (63.0%)	341 (59.0%)	0.371
LN+	128 (44.3%)	106 (36.7%)	234 (40.5%)	
Unknown	2 (0.7%)	1 (0.3%)	3 (0.5%)	
Grade				
G1	46 (15.9%)	42 (14.5%)	88 (15.2%)	0.995
G2	182 (63.0%)	190 (65.7%)	372 (64.4%)	
G3	58 (20.1%)	55 (19.0%)	113 (19.6%)	
Unknown	3 (1.0%)	2 (0.7%)	5 (0.9%)	

High Risk 2	AC-T (N=51)	TC (N=51)	Overall (N=102)	P-value
Age (Years)				
Mean (SD)	50 (± 11)	52 (± 11)	51 (± 11)	0.681
Menopausal Status				
Pre-/Peri-	23 (45.1%)	24 (47.1%)	47 (46.1%)	0.998
Post-	24 (47.1%)	22 (43.1%)	46 (45.1%)	
Unknown	4 (7.8%)	5 (9.8%)	9 (8.8%)	
Race				
AAPI	5 (9.8%)	2 (3.9%)	7 (6.9%)	
AIAN	0 (0%)	0 (0%)	0 (0%)	
Black	12 (23.5%)	6 (11.8%)	18 (17.6%)	
Latin American/Hispanic	2 (3.9%)	2 (3.9%)	4 (3.9%)	
Multiple	0 (0%)	0 (0%)	0 (0%)	
White	28 (54.9%)	39 (76.5%)	67 (65.7%)	0.645
Unknown	4 (7.8%)	2 (3.9%)	6 (5.9%)	
Tumor Stage				
T1	22 (43.1%)	31 (60.8%)	53 (52.0%)	0.456
T2	25 (49.0%)	19 (37.3%)	44 (43.1%)	
T3	3 (5.9%)	0 (0%)	3 (2.9%)	
T4	0 (0%)	0 (0%)	0 (0%)	
Unknown	1 (2.0%)	1 (2.0%)	2 (2.0%)	
Lymph Node Status				
LN-	27 (52.9%)	33 (64.7%)	60 (58.8%)	0.8
LN+	22 (43.1%)	16 (31.4%)	38 (37.3%)	
Unknown	2 (3.9%)	2 (3.9%)	4 (3.9%)	
Grade				
G1	1 (2.0%)	6 (11.8%)	7 (6.9%)	0.352
G2	16 (31.4%)	19 (37.3%)	35 (34.3%)	
G3	34 (66.7%)	25 (49.0%)	59 (57.8%)	
Unknown	0 (0%)	1 (2.0%)	1 (1.0%)	

Data presented as n (%) unless indicated otherwise; Unknown values excluded; P values of less than 0.05 were considered significant;
Abbreviations: N, sample size; SD, standard deviation; AAPI, Asian American and Pacific Islander; AIAN, American Indian or Alaska Native

Tables 3-4. Univariate and Multivariate Cox Proportional Hazards

Association of Clinical Variables on IDFS among High Risk 1			
Variable		**HR (univariable)**	**HR (multivariable)**
Age	Mean (SD)	1.02 (0.99-1.05, p=0.146)	1.02 (0.99-1.05, p=0.221)
Tumor Stage	T1	ref	ref
	T2/3	4.43 (1.98-9.95, p<0.001)*	4.05 (1.74-9.43, p=0.001)*
Lymph Node Status	LN-	ref	ref
	LN+	1.42 (0.80-2.54, p=0.232)	1.16 (0.63-2.14, p=0.632)
Grade	Non G3	ref	ref
	G3	1.09 (0.54-2.21, p=0.800)	1.12 (0.55-2.26, p=0.758)
Chemo Regimen	TC	ref	ref
	AC-T	1.01 (0.57-1.80, p=0.980)	0.99 (0.52-1.67, p=0.812)

Association of Clinical Variables on IDFS among High Risk 2			
H2 IDFS		**HR (univariable)**	**HR (multivariable)**
Age	Mean (SD)	1.03 (0.96-1.11, p=0.383)	1.02 (0.94-1.10, p=0.676)
Tumor Stage	T1	ref	ref
	T2/3	0.92 (0.21-4.12, p=0.916)	1.20 (0.22-6.54, p=0.836)
Lymph Node Status	LN-	ref	ref
	LN+	1.30 (0.29-5.81, p=0.734)	1.39 (0.22-8.84, p=0.730)
Grade	Non G3	ref	ref
	G3	0.26 (0.05-1.34, p=0.107)	0.30 (0.05-1.65, p=0.165)
Chemo Regimen	TC	Ref	ref
	AC-T	0.16 (0.02-1.29, p=0.048)*	0.18 (0.02-1.57, p=0.120)

Data presented as Hazard Ratio (95% CI, p-value).
P values of 0.05 or less were considered significant.

Results

- Among all paatients, 1,106 had H1 and 153 had H2 HR+HER2- breast cancer
- PSM resulted in no significant differences in clinical/pathologic features between the two chemotherapy groups within each H1 and H2 cohort (Tables 1-2)
- For patients with H1 BC, no significant difference in 3-yr IDFS was observed between AC-T (95.6%) and TC (94.6%) treatment (p = 0.98) (Figure 1)
  - The non-significant absolute difference in IDFS for patients with H1 tumors at 4- and 5-years remained <1%
- In contrast, H2 patients treated with TC had a significantly worse 3-yr IDFS of 89.3% compared with 100% for AC-T-treated patients, with an absolute benefit of 10.7% (p = 0.048) (Figure 2)
  - At 4- and 5-years the absolute differences in IDFS for patients with H2 cancers were 8.1% and 13.7%, respectively, in favor of AC-T treatment
- Multivariate Cox regression analysis within the H1 group showed no association with improved IDFS with AC-T, while the use of AC-T in patients with H2 showed a trend towards improved IDFS compared to TC, but did not reach significance likely due to sample size (Tables 3-4)

Conclusions

- In this PSM analysis of a non-randomized, prospective, real-world FLEX Study data with 3.2 years median follow-up, patients with H2, HR+HER2- cancer had significantly improved IDFS with AC-T compared to TC
- Although adjusted analyses were limited by few events, the direction and magnitude of benefit remained consistent
- In contrast, patients with H1 cancer did not benefit more from AC-T vs. TC
- These findings further support the utility of MammaPrint in informing chemotherapy selection in patients with HR+HER2- breast cancer

References: [1] Geyer et al., J Clin Oncol 2024 . [2]Brufsky, et al., JNCI Cancer Spectrum, 2025. [3]O'Shaughnessy, et al; J Clin Oncol 42, 2024 (suppl 16; abstr 511). [4]Tolaney, et al., J Clin Oncol 2021