Association of ImPrintTN signature with survival outcomes by race in Basal-Type Triple negative breast cancer (TNBC): FLEX registry analysis

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Introduction

- Black patients are disproportionately affected by triple negative breast cancer (TNBC) and experience worse clinical outcomes compared to non-Black patients[1]
- There is lack of data on racial differences in tumor biological factors in TNBC and how these differences may impact survival outcomes
- Previous research has shown that compared to non-black patients, Black patients with TNBC have enriched stromal tumor infiltrating lymphocytes (sTILs) that may be associated with higher rates pathological complete response (pCR) to neoadjuvant chemotherapy (CT) + immunotherapy (IO)[2]
- ImPrintTN is a 24 gene immune classifier signature for TNBC which is being prospectively evaluated in the ongoing I-SPY2.2 trial[3]
- **Objective:** Utilize Real-World Data (RWD) from FLEX (NCT03053193) to assess the association of ImPrintTN with self-reported race and its impact on survival outcomes in early stage, genomically BluePrint Basal-Type, TNBC

Methods

Patient population: Prospective, observational FLEX Registry (NCT03053193), receiving MammaPrint Risk testing (UltraLow, Low, High 1, or High 2) as standard-of-care

- Stage I-III TNBC (0% ER, 0% PR, and HER2 negative)
- Basal-Type by BluePrint, 80-gene molecular subtyping signature
- Self-report Black or White race (other races excluded from analysis due to small sample size of <10% in the enrolled population)
- Diagnosed between 2017 and 2024 with available survival data

Analysis: ImPrintTN (+/-) results acquired through whole transcriptome profiling

- Chi-squared and Fisher's exact tests assessed differences in clinical characteristics
- Association of pCR and ImPrintTN+/- were tested by binary logistic regression. Recurrence-free survival (RFS) per STEEP 2.0 criteria[4] was compared between race and ImPrintTN+/- using Kaplan-Meier estimates and log rank tests
- Cox proportional hazards model was used to analyze the association of ImPrintTN, race, and clinical features with RFS

References: 1. Dietze et al., Nat Rev Cancer, 2015; 2. Stecklein et al., Cancer Res, 2023, 83 (5_Supplement): PD1-06; 3. Wolf et al., EBCC, 2024; 4. Tolaney et al., JCO, 2024

Results

Table 1. Clinical Characteristics

	Black (N=66)	White (N=213)	Overall (N=279)	P-value
Age (Years)				
Mean (SD)	56 (± 14)	60 (± 13)	59 (± 13)	0.064
Menopausal Status				
Pre-/Peri-	17 (25.8%)	44 (20.7%)	61 (21.9%)	0.358
Post-	45 (68.2%)	165 (77.5%)	210 (75.3%)	
Unknown	4 (6.1%)	4 (1.9%)	8 (2.9%)	
Tumor Stage				
T1	25 (37.9%)	97 (45.5%)	122 (43.7%)	0.626
T2	28 (42.4%)	79 (37.1%)	107 (38.4%)	
T3	8 (12.1%)	12 (5.6%)	20 (7.2%)	
T4	2 (3.0%)	4 (1.9%)	6 (2.2%)	
Unknown	3 (4.5%)	21 (9.9%)	24 (8.6%)	
Lymph Node Status				
LN-	38 (57.6%)	149 (70.0%)	187 (67.0%)	0.151
LN+	26 (39.4%)	50 (23.5%)	76 (27.7%)	
Unknown	2 (3.0%)	14 (6.6%)	16 (5.3%)	
Grade				
G1	3 (4.5%)	5 (2.3%)	8 (2.9%)	0.943
G2	8 (12.1%)	34 (16.0%)	42 (15.1%)	
G3	53 (80.3%)	168 (78.9%)	221 (79.2%)	
Unknown	2 (3.0%)	6 (2.8%)	8 (2.9%)	
Treatment Type				
NeoCT	34 (55.7%)	105 (52.2%)	139 (53.1%)	0.959
AdjCT	25 (41.0%)	91 (45.3%)	116 (44.3%)	
Immunotherapy	2 (3.3%)	5 (2.5%)	7 (2.7%)	
MammaPrint				
Low	0 (0%)	1 (0.5%)	1 (0.4%)	1
High1	8 (12.1%)	27 (12.7%)	35 (12.5%)	
High2	58 (87.9%)	185 (86.9%)	243 (87.1%)	
ImPrintTN				
Positive	40 (60.6%)	118 (55.4%)	158 (56.6%)	0.761
Negative	26 (39.4%)	95 (44.6%)	121 (43.4%)	
Chemo Regimen				
TC	12 (18.2%)	37 (17.4%)	49 (17.6%)	0.840
AC	3 (4.5%)	5 (2.3%)	8 (2.9%)	
AC-T	23 (34.8%)	99 (46.5%)	122 (43.7%)	
Chemo+Platinum	18 (27.3%)	38 (17.8%)	56 (20.1%)	
Other	4 (6.1%)	9 (4.2%)	13 (4.7%)	
Unknown	6 (9.1%)	25 (11.7%)	31 (11.1%)	

TC, taxane + cyclophosphamide ; AC-T, anthracyclines and taxanes

Figure 1. Association of pCR with Race and ImPrintTN+/-

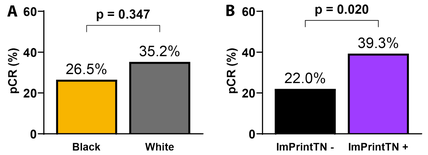
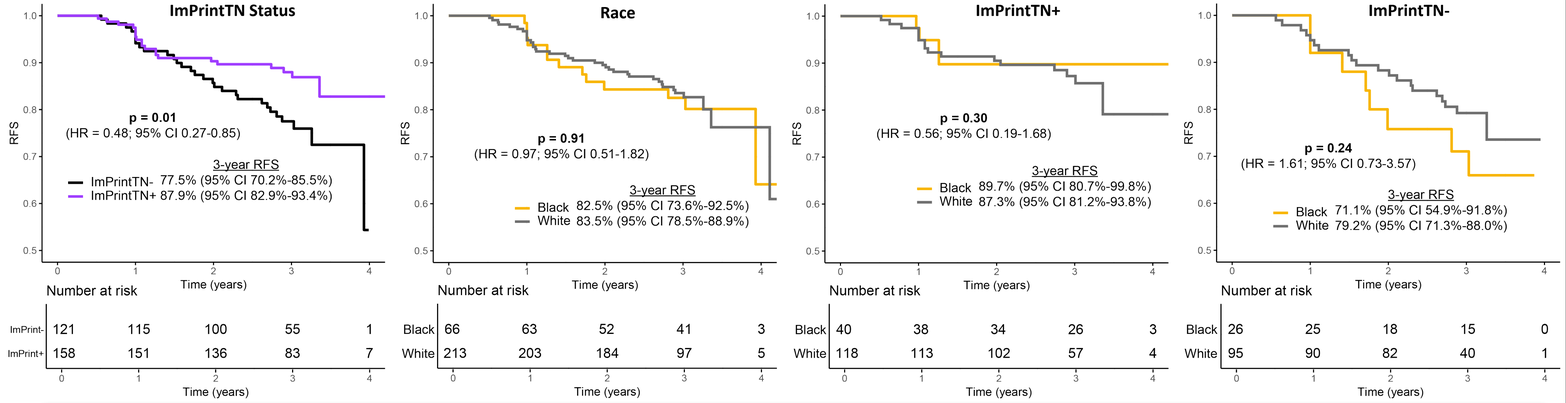


Figure 2. ImPrintTN+ status was prognostic of recurrence-free survival among Black and White patients enrolled in FLEX with BluePrint Basal-Type, TNBC



- Among 279 patients, 23.7% were Black and 76.3% were White (**Table 1**)
  - Similar proportions of Black and White patients had MammaPrint High 2 tumors, while the ImPrintTN+ rate was numerically higher among Black patients
  - Most patients received anthracycline and/or platinum-containing chemotherapy regimens
- ImPrintTN was associated with pCR, whereas there was no association of race with pCR (**Figure 1**)
- On Multivariate Logistic regression (adjusting for meno status, race, T stage, LN+/-, and grade), ImPrintTN+ status continued to be predictive of higher pCR (OR=2.38, 95% CI 0.98-6.14, p=0.042)
- Significantly improved 3-year RFS was associated with ImPrintTN+ (87.9%) compared to ImPrintTN- (77.5%; p=0.01; **Figure 2**)
- 3-year RFS was similar for Black (82.5%) and White (83.5%; p=0.91) patients
- RFS was similar for Black (89.7%) and White (87.3%; p=0.30) patients with ImPrintTN+
- ImPrintTN- observed a trend towards lower 3-year RFS in Black (71.1%) compared with White (79.2%; p=0.24) patients
- ImPrintTN+ and LN+ was associated with RFS in a multivariate model (**Table 2**)

Table 2. Univariate and multivariate analysis of ~~clinical~~ factors associated with RFS

Variable		HR (univariable)	HR (multivariable)
ImPrintTN	Negative		ref
	Positive	**0.48 (0.27-0.85, p=0.012)**	**0.41 (0.22-0.75, p=0.004)**
Race	White	ref	ref
	Black	0.97 (0.51-1.82, p=0.912)	1.01 (0.52-1.97, p=0.977)
Lymph Node Status	LN-	ref	ref
	LN+	**2.93 (1.64-5.23, p<0.001)**	**2.98 (1.66-5.37, p<0.001)**
Treatment Type	Adjuvant	ref	ref
	Neoadjuvant	1.15 (0.65-2.04, p=0.621)	1.00 (0.54-1.85, p=0.993)

Conclusions

- To our knowledge, this is the first study assessing the prognostic impact of ImPrintTN on survival among patients with TNBC
- In the FLEX Registry, Black and White patients with genomically Basal TNBC had similar proportions of MammaPrint High 2 tumors (87.9% vs 86.9%), while ImPrintTN+ cancers were numerically higher in Black patients (60.6% vs 55.4%)
- ImPrintTN+ status was predictive of pCR and independently prognostic for RFS
- ImPrintTN- status was associated with sub-optimal RFS (3-year RFS of 77%)
  - Notably, the negative prognostic impact of ImPrintTN- status appeared more pronounced among Black compared with White patients
- Ongoing research efforts will focus on
  - Exploring biological differences within the ImPrintTN- subgroup by race
  - Updating this analysis as the FLEX Registry of Real-World Data continues to enroll more patients who have received chemo-immunotherapy