Exploring Potential Predictive Factors for Immunotherapy Response in Early-Stage TNBC: Insights from a Retrospective Analysis

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Background

NACT-IO has been the SOC for high-risk early-stage triple-negative breast cancer (eTNBC) for over 5 years.

Data on predictive biomarkers and clinical factors associated with treatment response remains limited. This study evaluates the association of several factors with pCR following NACT-IO.

1. BRCA1/2 mutations, present in ~15-20% of TNBC cases, are linked to higher TMB, potentially enhancing immunotherapy response.
2. Angiotensin-converting enzyme (ACE) is intrinsically expressed in immune cells and may influence anti-tumor immunity.
3. irAEs occur in ~30% of eTNBC patients receiving NACT-IO; while higher-grade irAEs have been linked to improved pCR, data on low-grade irAEs remain limited.

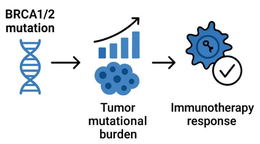
Thus, we assessed how BRCA1/2 status, ACE inhibitor use, and irAE severity may impact response to NACT-IO.

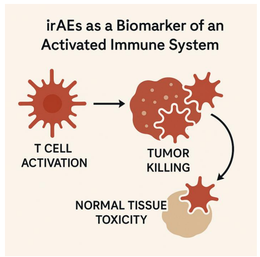
Methods and materials

A retrospective analysis including eTNBC patients treated with NACT-IO at the Henry Ford Health System between July 2021 and October 2024.

Categorical variables were analyzed using Chi-square or Fisher exact tests; $P < 0.05$ was considered significant.

Biologically plausible theories





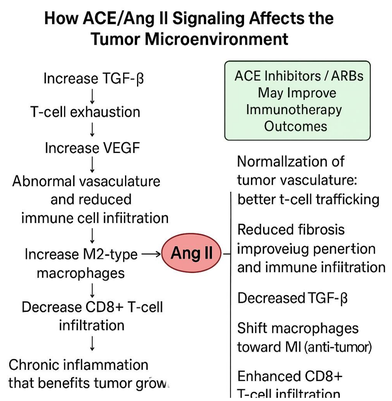


Table 1. Clinical Factors and Surgical Outcomes

		Surgical Outcome: Residual Disease (N=67)	Surgical Outcome: pCR (N=93)	Comparison P-value	Cramér's V (Effect size)
Mutation Status	BRCA1/BRCA2	3 (21.4%)	11 (78.6%)	0.265 (C)	0.09 (small)
	Non-Mutated	47 (43.5%)	61 (56.5%)		
	Unknown	17 (44.7%)	21 (55.3%)		
ACE Inhibitor use	No	57 (42.9%)	76 (57.1%)	0.749 (C)	0.005 (None)
	Yes	7 (38.9%)	11 (61.1%)		
Grade of Side Effect (no irAE or G 1 versus G 2, 3, or 4)	No irAE or G 1	56 (51.4%)	53 (48.6%)	<0.001 (C)	0.27 (Medium)
	G2, 3, 4	11 (21.6%)	40 (78.4%)		

(C) = Chi-Square Test

Results

Among 173 eligible patients:
- 14 (8%) had pathogenic BRCA1/2 mutations
- 18 (10%) were on ACE inhibitors
- 7 (4%) had grade 1 irAEs
- 51 (29%) had grade ≥2 irAEs.

- pCR rates were higher among those with grade ≥2 irAEs versus those with grade 1 or no irAEs.
- No significant differences in pCR rates were seen by BRCA status or ACE inhibitor use.
- BRCA-mutated patients showed a numerical trend toward higher pCR rates.

Conclusions

- ✓ pCR rates were significantly higher in patients with grade ≥2 irAEs.
- ✓ The low number of grade 1 irAEs may reflect underreporting.
- ✓ While BRCA1/2 mutation carriers had numerically higher pCR rates, this was not statistically significant, suggesting a potential improvement in response that warrants further study.
- ✓ ~22% of patients lacked documented BRCA status, underscoring the need for universal genetic testing in TNBC.
- ✓ No significant association was found between ACE inhibitor use and surgical outcomes; however, larger studies are needed to clarify their potential impact on response to immunotherapy.

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