Risk Stratification and Relapse Pattern in Triple-Negative Breast Cancer with Pathological Complete Response after Neoadjuvant Treatment: The European GAMBIT Real-world Study

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San Antonio Breast Cancer Symposium
December 9-12, 2025. ID #3070

INTRODUCTION

- **Pathological complete response (pCR)** after **neoadjuvant** treatment (NAT) associates with improved outcomes in triple-negative breast cancer (TNBC), **yet 10% of patients experience relapse.**
- **Tumor infiltrating lymphocytes (TILs)** are positive independent **prognostic biomarker** in **TNBC**

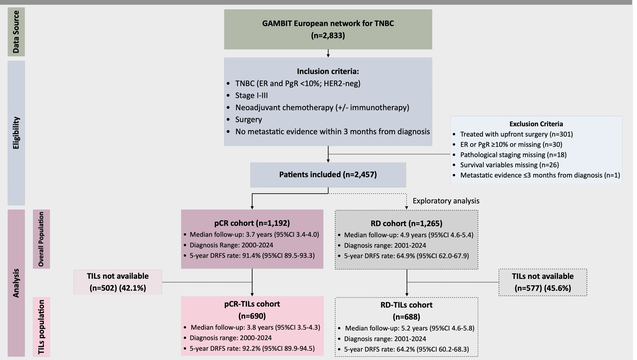
OBJECTIVES

1) Do **TILs** allow do identify those **patients with pCR with residual risk of relapse?**
2) Do patients with **pCR** have the **same pattern of relapse** as those with **residual disease?**

METHODS

- Survival endpoints: distant-relapse free survival (DRFS) and overall survival (OS)
- TILs were modeled as a linear term (5% incr.) and predefined ≥30% cut-off (high-TILs)
- Site of first distant relapse sites were recorded; central-nervous system (CNS) with extracranial disease was classified as CNS-any, without as CNS-only.
- Cumulative incidence functions were compared by Gray's test.

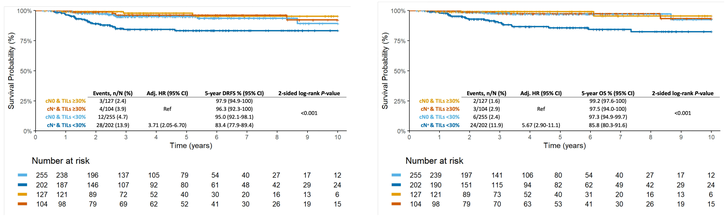
STUDY COHORTS



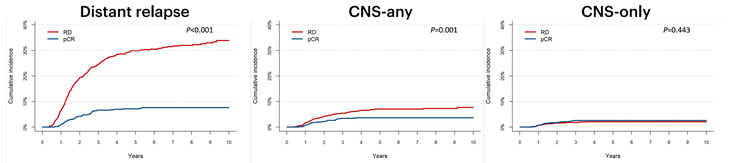
RESULTS

		pCR Cohort N = 1,192	RD cohort N = 1,265	P-value
Age at diagnosis, years	Median (IQR)	49 (41-58)	51 (42-61)	**<0.001**
Histology, n (%)	Ductal	1,076 (94.6%)	1,109 (91.7%)	**0.005**
	Lobular	8 (0.7%)	25 (2.1%)	
	Others	54 (4.7%)	76 (6.3%)	
ER status, n (%)	<1	1,089 (91.4%)	1,161 (91.8%)	0.7
	≥1-9 (ER-low)	103 (8.6%)	104 (8.2%)	
Grade, n (%)	1	1 (0.1%)	2 (0.2%)	**<0.001**
	2	104 (9.4%)	218 (18.5%)	
	3	1,006 (90.5%)	961 (81.4%)	
Ki67	Median (IQR)	70 (50-80)	60 (40-80)	**<0.001**
TILs	Median (IQR)	15 (5-35)	10 (5-25)	**<0.001**
cT, n (%)	0	6 (0.5%)	9 (0.7%)	**<0.001**
	1	215 (18.9%)	172 (13.7%)	
	2	721 (63.2%)	715 (56.8%)	
	3	152 (13.3%)	255 (20.3%)	
	4	45 (4.0%)	107 (8.5%)	
cN, n (%)	Negative	678 (57.1%)	637 (50.6%)	**0.001**
	Positive	510 (42.9%)	621 (49.4%)	
Neoadjuvant Regimen, n (%)	Chemotherapy	545 (45.7%)	845 (66.8%)	**<0.001**
	Chemotherapy including Carboplatin	260 (21.8%)	249 (19.7%)	
	Chemotherapy + Immunotherapy	387 (32.5%)	171 (13.5%)	
Neoadjuvant chemotherapy backbones, n (%)	Anthracyclines	1,146 (96.4%)	1,182 (93.7%)	**0.002**
	Taxanes	1,092 (92.0%)	1,121 (88.9%)	**0.009**
	Carboplatin	643 (54.0%)	416 (32.9%)	**<0.001**

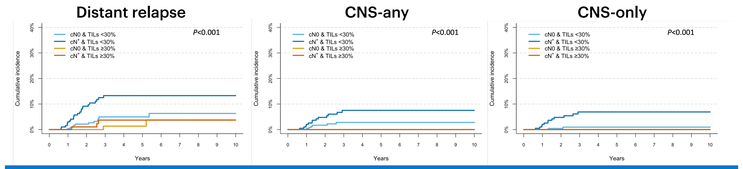
PROGNOSTIC STRATIFICATION in pCR: Nodal status and TILs



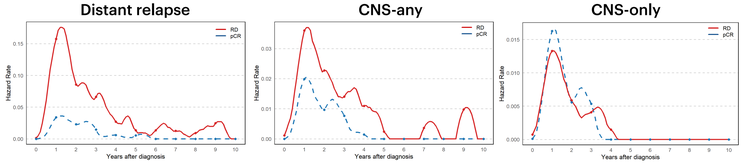
PATTERN OF RELAPSE: pCR vs RD



PATTERN OF RELAPSE: pCR according to cN/TILs



SMOOTHED SITE-SPECIFIC HAZARD RATE in pCR vs RD



CONCLUSIONS

- In TNBC, **pCR is prognostically heterogeneous:** cN and TILs stratify this risk.
- Patients with **pCR and RD: similar cumulative incidence** of **CNS-only relapse** (2.6% vs 2.1%)
- Among patients with pCR, **cN+/low-TILs** are at **increased risk of CNS relapse** (5-yr cumulative incidence of CNS-only: 6.9%)
- Our results support **risk-adapted allocation** of **patients with high-risk pCR** in clinical trials of **CNS-active agents** (e.g. antibody-drugs conjugates) and CNS surveillance.

KEY CLINICAL SIGNALS

pCR ≠ cure
cN+/low-TILs 5-year DRFS 83%, OS 86%.

pCR and RD: similar CNS-only relapse

ACKNOWLEDGEMENTS



Funding: Associazione Italiana per la Ricerca sul Cancro (IG 27152 to Prof. M.V. Dieci; ID22759 to Prof. V. Guarneri).

Ref: Miglietta F. et al CTR 2022; Spring LM et al. CCR 2020; Loi S. et al JCO 2019; Denkert C. Lancet 2018

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