Rare but Resistant: Neoadjuvant Chemoimmunotherapy in Special Histological Subtypes of Triple-Negative Breast Cancer — Insights from the Neo-Real/GBECAM-0123 Study

R. Barroso-Sousa[1], L. Testa[2], P. Mandó[3], M. C. Tavares[4], N. C. Nunes[5], G. Cordoba[3], F. Waisberg[3], F. C. Balint[4], I. M. de Sousa[6], M. O. Andrade[1], M. C. Gouveia[7], F. Madasi[8], J. Bines[8], R. P. Ferreira[9], D. D. Rosa[9], C. L. Santos[10], M. R. Monteiro[11], Z. S. de Souza[12], D. Assad-Suzuki[12], C. dos Anjos[13], D. M. Gagliato[14], A. U. Gomes[14], B. M. Zucchetti[7], A. Ferrari[15], M. L. de Brito[16], M. F. Monteiro[17], P. A. Signorini[18], N. J. Gomes[19], C. Gallina[3], S. Sanches[4], P. M. Hoff[20], M. Estevez-Diz[21], R. C. Bonadio[20]

[1]Oncology, Brasilia Hospital, Oncologia Américas, Brasilia, BRAZIL, [2]Oncology, Instituto D'Or de Pesquisa e Ensino, Brasilia, BRAZIL, [3]Oncology, SUMA (Grupo Cooperativa Argentino para el estudio y la investigación del Cáncer de Mama), Buenos Aires, ARGENTINA, [4]Oncology, A.C.Camargo Cancer Center, São Paulo, BRAZIL, [5]Oncology, Grupo Américas, Rio de Janeiro, BRAZIL, [6]Oncology, A.C.Camargo Cancer Center, Brasilia, BRAZIL, [7]Oncology, Hospital 9 de Julho, Grupo Américas, São Paulo, BRAZIL, [8]Oncology, Instituto D'Or de Pesquisa e Ensino, Rio de Janeiro, BRAZIL, [9]Oncology, Hospital Moinhos de Vento, Porto Alegre, BRAZIL, [10]Oncology, Instituto D'Or de Pesquisa e Ensino, Recife, BRAZIL, [11]Oncology, Grupo Américas, Hospital Samaritano, São Paulo, BRAZIL, [12]Oncology, Hospital Sírio-Libanês, Brasilia, BRAZIL, [13]Oncology, Hospital Sírio-Libanês, São Paulo, BRAZIL, [14]Oncology, Hospital Beneficência Portuguesa, São Paulo, BRAZIL, [15]Oncology, Hospital Santa Paula, Grupo Américas, São Paulo, BRAZIL, [16]Oncology, Clínica AMO, Salvador, BRAZIL, [17]Oncology, Instituto do Câncer do Ceará, Fortaleza, BRAZIL, [18]Oncology, Centro Integrado de Pesquisa da Amazônia (CINPAM), Manaus, BRAZIL, [19]Oncology, Hospital São Domingos, DASA Oncologia, São Luiz, BRAZIL, [20]Oncology, Instituto D'Or de Pesquisa e Ensino, São Paulo, BRAZIL, [21]Oncology, Instituto do Câncer do Estado de São Paulo, Faculdade de Medicina da Universidade de São Paulo, São Paulo, BRAZIL.

Introduction

Special histological types (SHT) of triple-negative breast cancer (TNBC) exhibit distinct biological behavior and treatment responses. However, due to their rarity, patients with SHT are underrepresented in clinical trials. We aimed to evaluate the effectiveness of pembrolizumab (P) combined with neoadjuvant chemotherapy (NCT) in patients with SHT of TNBC.

Methods

- Multicentric real-world analysis of patients with early-stage TNBC treated with neoadjuvant pembrolizumab plus chemotherapy at ten cancer centers since July 2020.
- Effectiveness outcomes included pathologic complete response (pCR) and event-free survival (EFS).

Results

Flow chart of patients included in the study

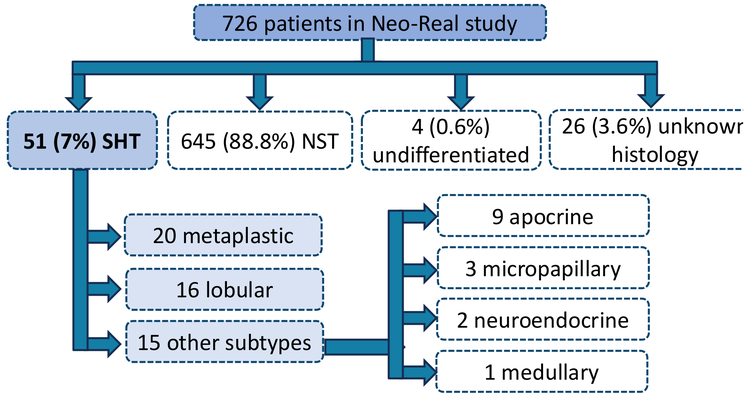
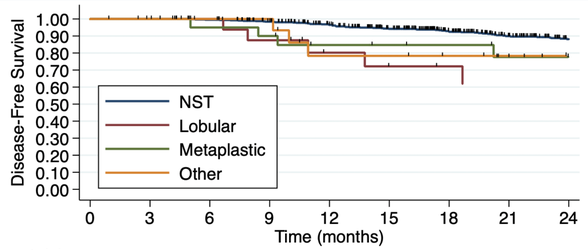


Table 1. Patients' characteristics

Variable	Metaplastic (N=20)	Lobular (N=16)	Other SHT (N=15)	NST (N=645)	P-value
Age, median (range)	51 (22-74)	58 (40-82)	49 (38-80)	44 (21-91)	**0.003**
Premenopausal	7 (39%)	2 (17%)	7 (47%)	299 (54%)	0.114
Stage II III	 15 (75%) 5 (25%)	 12 (80%) 3 (20%)	 8 (53%) 7 (47%)	 456 (73%) 169 (27%)	0.380
Grade 3 (%)	16 (84%)	7 (50%)	7 (50%)	461 (76%)	**0.018**
Ki-67 ≥50% (%)	10 (53%)	8 (53%)	5 (36%)	474 (76%)	**<0.001**
BRCA mutated (%)	2 (10%)	2 (12%)	0 (0%)	97 (15%)	0.461
AC schedule Every 3 weeks Dose-dense	 9 (47%) 10 (53%)	 8 (57%) 6 (43%)	 7 (50%) 7 (50%)	 291 (47%) 332 (53%)	0.914

Disease-free survival in NST vs rare histologic subtypes of TNBC



Number at risk

NST	644	639	626	599	554	493	413	338	279
Lobular	16	16	16	14	10	8	7	6	6
Metaplastic	20	20	19	18	15	14	13	9	5
Other	15	15	15	15	10	10	8	7	6

Table 2. pCR and EFS of special histological types

	pCR	OR (95% CI)	2-year EFS	HR (95% CI)
NST	64.7%	ref	88.0%	ref
Lobular	69.2%	1.22 (0.37-4.04)	61.9%	**3.98 (1.60-9.89)**
Metaplastic	16.7%	**0.10 (0.031-0.38)**	77.7%	**2.67 (1.07-6.63)**
Other SHT	46.2%	0.46 (0.15-1.41)	78.3%	2.26 (0.71-7.21)

- pCR rates were markedly lower in metaplastic tumors compared to NST and lobular subtypes.
- With a median follow-up of 22 months, 83 events of disease recurrence or death were recorded. Lobular and metaplastic tumors were associated with significantly lower 2-year EFS compared to NST.
- These differences remained significant in a multivariable Cox regression including tumor grade and stage (Table 2).
- Disease progression during P+NCT was significantly higher in the metaplastic group (33%) compared to NST (3%) and lobular tumors (0%) (p = 0.001). However, all but one patient with progression in the metaplastic group underwent surgery.

CONCLUSIONS

1. Patients with SHT had worse outcomes with P+NCT compared to those with NST tumors.
2. Metaplastic carcinoma was associated with lower pCR and lower EFS rates.
3. Although lobular carcinoma had pCR rates similar to NST, an unfavorable EFS was also observed in this group.
4. These results underscore the need for developing new tailored therapeutic strategies for these rare subtypes of TNBC.

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