Immune-related adverse events and pathological complete response in early TNBC treated with neoadjuvant chemo-immunotherapy: a real-world analysis

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Summary / Objective

This study investigated the **incidence and clinical significance of immune-related** adverse events (irAEs) **in patients with early-stage triple-negative breast cancer (TNBC)** treated with **neoadjuvant chemo-immunotherapy (Ch-IT)** in a real-world setting. Nearly half of the patients (46.8%) experienced irAEs, leading to treatment discontinuation in 36.4% of cases. Although no statistically significant correlation between irAEs and pathological complete response (pCR) was observed, patients who developed grade ≥3 irAEs more frequently achieved pCR, **suggesting a potential link between immune activation and therapeutic efficacy**. These findings underscore the need to better characterize irAEs as potential predictive biomarkers of response and to optimize toxicity management to ensure treatment continuity and maximize clinical benefit.

Introduction

TNBC is the most aggressive breast cancer subtype. After the KEYNOTE-522 trial showed improved pCR rates, neoadjuvant Ch-IT became standard of care. However, real-world data on tolerability and irAEs remain limited. This study evaluates the efficacy and safety of Ch-IT in early-stage TNBC, focusing on the association between irAEs and pCR.

Table 1. Baseline clinical and pathological characteristics stratified by pCR status .

Variable	Total population n = 77	pCR n = 47	Non pCR n =30
Mean age (+SD)	52 (±10.8)	52.5 (±10.9)	51.2 (±10.9)
T stage			
1	12 (15.6%)	7	5
2	50 (64.9%)	31	19
3	11 (14.3%)	5	6
4	2 (2.6%)	2	0
x	2 (2.6%)	2	0
N stage			
0	41 (53.2%)	24	17
1	25 (32.5%)	15	10
2	10 (13%)	7	3
3	1 (1.3%)	1	0
RCB			
0	47 (61%)	47	0
I	10 (13%)	0	10
II	13 (16.9%)	0	13
III	4 (5.2%)	0	4
NA	3 (3.9%)	0	3
Neoadyuvant treatment interruption			
Yes	28 (36.4%)	17	11
No	49 (63.6%)	30	19
IRAEs (any grade)			
Yes	36 (46.8%)	24	12
No	41 (53.2%)	23	18

Methods and Materials

We conducted a **retrospective analysis** of medical records from **77 patients** with *early-stageTNBC > 2 cm* and/or lymph node positive who received neoadjuvant Ch-IT between *January 2023 and November 2024*. Endpoints were the rate of **pCR** (defined as absence of invasive cells in breast and lymph nodes), **rate of treatment discontinuation** prior to surgery, incidence of **irAEs** (graded according to CTCAE v5.0) and their **association** with pCR.

Results

A pCR was achieved in 47 patients (61%). Baseline clinical and pathological characteristics stratified by pCR status are shown in Table 1. **Neoadjuvant treatment was permanently discontinued before surgery in 28 patients (36.4%) all attributable to Ch-IT toxicity**. A total of 36 patients (**46.8%) experienced irAEs** detailed in Table 2. **No** statistically significant **association** was observed between the occurrence of irAEs and achieving a pCR ($\chi^2 = 0.9$; *p = 0.34*); however, **6 of the 8 patients who developed grade ≥3 irAEs achieved a pCR.**

Table 2. Immune-related adverse events in the total population.

	Any grade	Grade ≥3
Hipothyroidism	18 (23.4%)	0
Hepatitis	10 (13%)	3 (3.9%)
Colitis	7 (9.15)	2 (2.6%)
Pneumonitis	4 (5.2%)	0
Arthritis	3 (3.9%)	0
Hyperthyroidism	2 (2.6%)	0
Adrenal insufficiency	4 (5.2%)	1 (1.3%)
CK elevation	1 (1.3%)	1 (1.3%)
Neurological	1 (1.3%)	1 (1.3%)
Skin rash	1 (1.3%)	0

Conclusions

In this **real-world cohort** of patients with early-stage TNBC, neoadjuvant Ch-IT demonstrated a pCR rate consistent with the KEYNOTE-522 trial. **Although no statistically significant association was found between irAEs and pCR, a numerical trend was observed, particularly among patients with grade ≥3 events**. Further studies with larger cohorts are warranted to elucidate the potential predictive role of irAEs in treatment response and long-term outcomes.

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