Clinicopathological features and outcomes of triple-negative breast cancer relapsing after pembrolizumab-based neoadjuvant therapy

Authors : Kabirian R[1], Gendreau M[1], Bidard FC[1], Lerebours F[1], Vincent Salomon A[2], Djerroudi L[2], Cottu P[1], Coussy F[1], Pierga JY[1], Cabel L[1], Loirat D[1]
[1]Department of Medical Oncology & [2]Department of Pathology-Genetics and Immunology, Institute of Women's Cancers Institut Curie, Paris and Saint-Cloud, France

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BACKGROUND

Neoadjuvant chemo-immunotherapy (NACI) based on pembrolizumab in combination with paclitaxel and carboplatin followed by anthracycline and cyclophosphamide has become the standard of care for stage II-III triple-negative breast cancer (TNBC)[1,2,3]. However, clinicopathological features and outcomes of metastatic relapse after NACI remain poorly documented.

OBJECTIVES

This study aimed to describe progression-free survival on first-line metastatic therapy (**PFS1**) and overall survival (**OS**) **in patients (pts) with TNBC relapsing after or progressing during NACI.** Clinicopathological features and treatment characteristics were analyzed.

METHODS

We conducted a retrospective analysis at Institut Curie Hospitals (France) including all pts diagnosed with localized TNBC, receiving **pembrolizumab - based neoadjuvant chemotherapy** and diagnosed with a metastatic relapse between 11.2022 and 05.2025.

Early relapse was defined as **unresectable tumor, or relapsing before completion of adjuvant treatement or within 6 months after end of adjuvant therapy.** Late relapse was defined as relapse ≥ 6 months after end of adjuvant therapy
PFS was defined on 1st line therapy (**PFS1**), overall survival **OS,** from date of distant metastatic relapse.

RESULTS

Among 429 ps who started NACI for early TNBC between 08.2021 and 11.2024, 33 women experienced metastatic relapse, disease progression during NACI, or progression during adjuvant treatment.

Table 1: Patients characteristics at baseline presentation (N=33)

History of Breast Cancer	4 (12.1%)
Germline mutation BRCA1/2	2/32 (6.1%)
Carcinoma of no specific type	27 (81.8%)
cT : 1-2	19 (57.6%)
3-4	14 (42.4%)
cN : N0	10 (30.3%)
N+	23 (69.7%)
HER2 (+) : 0	20 (60.6%)
1	9 (27.3%)
2 (negative FISH)	4 (12.1%)
TILs : <30%	25 (75.8%)
≥30%	8 (24.2%)
CPS score : 0-9	12 (36.4%)
10–100	15 (45.4%)
Unknown	6 (18.2%)

Table 2: RCB score after neoadjuvant chemo-immunotherapy

RCB 0	5 (16.1%)
1	4 (12.9%)
2	12 (38.7%)
3	10 (32.3%)
No surgery for progression	*2*

Figure 1 : Adjuvant medical treatment for early TNBC after NACI (N=29)

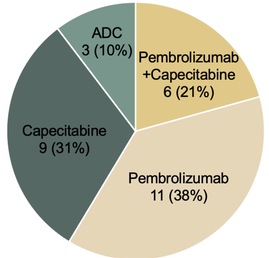


Table 3: Patients characteristics at progression or metastatic relapse (N=33)

At progression or metastatic relapse	**N = 33**
Age, median (min-max)	44 (28–75)
Performans status : 0	15 (45.5%)
1	16 (48.5%)
2	2 (6.1%)
Inoperable	2 (6.1%)
Resectable and progression	
before/during adjuvant therapy	10 (30.3%)
<6 months after end of adj.	12 (36.4%)
6–12 months after end of adj.	5 (15.2%)
>12 months after end of adj.	4 (12.1%)
Metastases: Visceral	23 (69.7%)
Bone-only	3 (9.1%)
Brain	6 (18.2%)
Prior local recurrence	2 (6.1%)
Concurrent local recurrence	10 (30.3%)

At data cuff of October 20th 2025, median follow-up from time of metastatic diagnosis was 11.8 months (IQR: 7.6–17). Median age at metastatic diagnosis was 44 years (min-max=28-75).
Pts received a median of 1 line (range 1-4), First –line treament consited of Sacituzumab Govitecan (SG) in 17 pts (52%), chemotherapy (CT) in 11 pts (33%), CT + Immunotherapy in 3 pts (9%) and other therapied (olaparib/trials) in 2 pts (6%).
27 pts experienced disease progression with a **median PFS1 of 3.9 months** [IQR: 1.7-5.2], 6 pts are still receiving first line treatment. Among the 16/27 pts (59%) who received a second line of treatment L2, 15 pts presented a progression.

Figure 2: PFS1 in whole cohort and by L1 type of treatment (N=33)

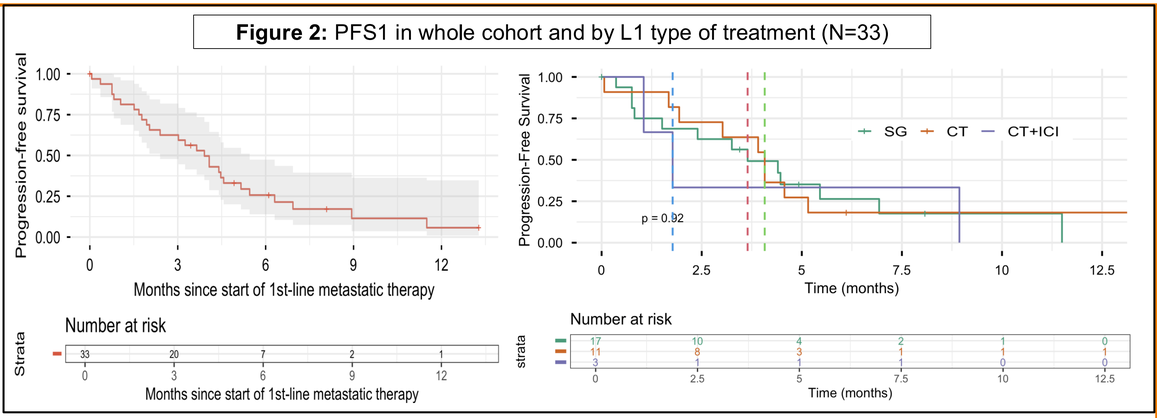
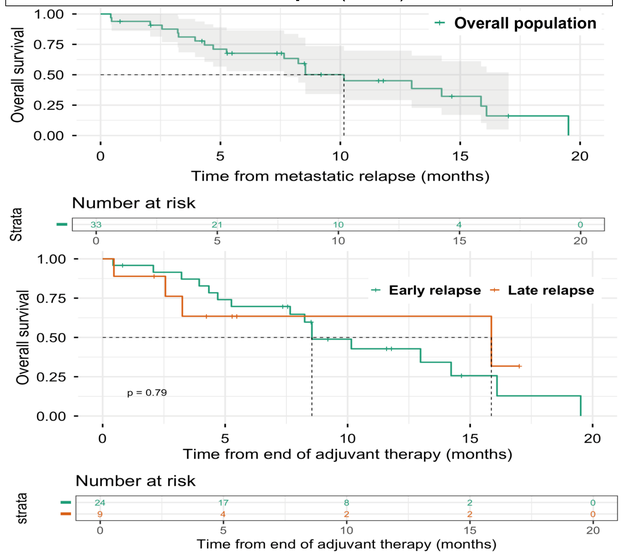


Figure 3: OS in whole cohort and and according to **early vs. late relapse** (N=33)



CONCLUSION

- **72% of pts relapsed within six months** after end of adjuvant therappy or before primary tumor surgery
- **59% of pts received a second line of treatment**
- **mPFS1 was 3.9 months, with a mOS of 10.2 months** from distant metastatic relapse, despite SG being the most frequent first-line therapy
- To increase the cohort size, an ambispective multicenter study will be conducted to more thoroughly characterize the tumor biology and patient outcomes of metastatic TNBC recurring after NACI.

REREFENCES

[1]R. Dent, Annals of Oncol, 2024; [2]A. Bardia, JCO, 2024; [3]P. Schmid, NEJM, 2020

CONTACT
Dr KABIRIAN Rayan, MD, medical gynecologist
rayan.kabirian@curie.fr