Clinical Outcomes of ER-Positive to Negative Conversion Versus TNBC: Evidence from a ^{18}F-FES PET/CT Guided Propensity-Score-Matched Study.

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Background

- Patients with estrogen receptor (ER)-positive breast cancer may experience ER-negative conversion (ER loss) during disease progression.
- ^{18}F-fluoroestradiol positron emission tomography/computed tomography (^{18}F-FES PET/CT) offers a practical approach for comprehensive ER evaluation across all metastatic sites, allowing early identification of ER conversion—especially valuable for cases where biopsy is technically challenging.
- This study aimed to compare survival outcomes and clinical characteristics between ER loss and metastatic triple-negative breast cancer (mTNBC) patients, exploring the prognostic implications of dynamic ER changes.

Methods

- This retrospective study screened 808 patients with ER-positive, HER2-negative breast cancer at initial diagnosis who underwent 18F-FES PET/CT after diagnosis of recurrent or metastatic disease from 2017 to 2023 at Fudan University Shanghai Cancer Center.
- Among them, 82 patients with functional ER loss detected by FES-PET at metastatic sites before first-line treatment were identified.
- 115 contemporaneous standard mTNBC patients with complete medical records were enrolled in control group.
- Propensity score matching (PSM) was used to balance baseline characteristics (number of metastatic sites, visceral/liver/lung/bone metastasis, taxane therapy history; caliper = 0.1).

Results

Baseline clinical characteristics

- PSM matched 59 patients per group and baseline clinical characteristics are well-balanced (Table 1). FES-PET showed 71.7% concordance with IHC.

Table 1. Demographic and baseline clinical characteristics after PSM.

Characteristics	After PSM (ER negative conversion vs mTNBC)		
	ER negative conversion Patients, No. (%)	mTNBC Patients, No. (%)	*P* value
n	59	59	
Age			
≤50	27 (45.8)	22 (37.3)	0.455
>50	32 (54.2)	37 (62.7)	
Disease-free interval			
De novo stage IV	5 (8.5)	11 (16.9)	0.179
ECOG score			
0	2 (3.4)	2 (3.4)	>0.999
≥1	57 (96.4)	57 (96.4)	
Number of metastatic sites			
1	20 (33.9)	20 (33.9)	>0.999
2	17 (28.8)	17 (28.8)	
≥3	22 (37.3)	22 (37.3)	
Metastatic sites			
Visceral	30 (50.8)	30 (50.8)	>0.999
Liver	6 (10.2)	7 (11.9)	>0.999
Lung	24 (40.7)	22 (37.3)	0.850
Bone	28 (47.5)	29 (49.2)	>0.999
HER2 status			
Negative	59 (100.0)	59 (100.0)	>0.999
Adjuvant/neo-adjuvant chemotherapy			
Taxanes	44 (74.6)	44 (74.6)	>0.999

Results

Effectiveness

- Median progression-free survival (PFS) was significantly shorter in ER loss group compared with mTNBC (6.7 vs 12.0 months, HR=1.55, P=0.042) (Figure 1).
- Overall survival (OS) data was immature.
- Objective response rate (ORR) (15.3% vs 37.3%) and disease control rate (DCR) (72.9% vs 84.7%, P=0.044) favored mTNBC, as well (Table 2 & Figure 2).

Figure 1. Kaplan-Meier plot of PFS in mTNBC and ER negative conversion group.

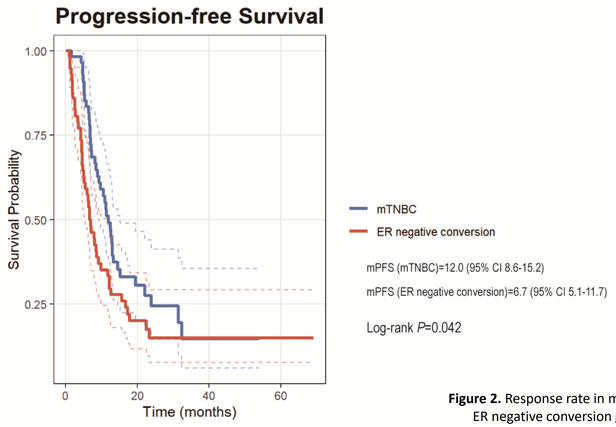
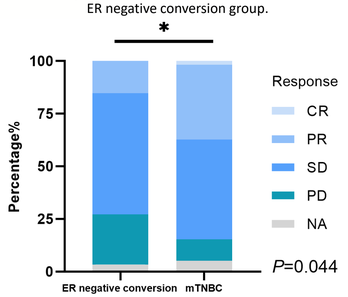


Table 2. Tumor response of study cohort.

	ER negative conversion (n=59)	mTNBC (n=59)
CR	0 (0.0)	1 (1.7)
PR	9 (15.3)	21 (35.6)
SD	34 (57.6)	28 (47.5)
PD	14 (23.7)	6 (10.2)
NA	2 (3.4)	3 (5.1)
ORR (after PSM)	15.3%	37.3%
DCR (after PSM)	72.9%	84.7%

Figure 2. Response rate in mTNBC and ER negative conversion group.



Results

Exploratory analysis

- Androgen receptor (AR) expression is available in 25 and 32 patients in ER loss and mTNBC group, respectively, and AR pathway positivity (≥10%) was significantly higher in ER loss group (88.0% vs 25.0%, P<0.0001) (Table 3 & Figure 3).

Figure 3. Androgen status in study cohort.

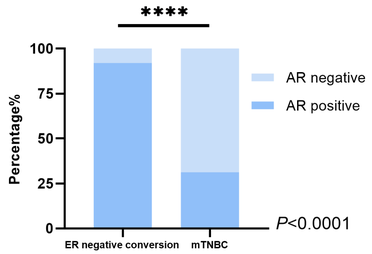
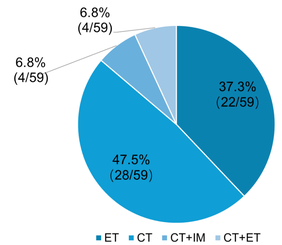


Figure 4. First-line systemic treatment of ER negative conversion patients.



- 28 of 59 (47.5%) ER loss patients received chemotherapy, and 18 of them received capecitabine based first-line therapy (Figure 4 & Table 4), while 34 of 59 (57.6%) mTNBC patients received platinum-based chemotherapy and 8 of 59 mTNBC patients had PD-1/PD-L1 exposure in first-line therapy (Table 5).

Table 3. Androgen status in mTNBC and ER negative conversion groups.

	ER negative conversion (n=25)	mTNBC (n=32)
AR positive	22 (88.0)	8 (25.0)
AR negative	3 (12.0)	24 (75.0)

Table 4. Chemotherapy regimen of first-line treatment in ER negative conversion patients.

	Chemotherapy regimen in the first-line treatment (n=28)
Capecitabine	18 (64.3)
Taxanes	10 (35.7)
Cisplatin/carboplatin	6 (21.4)
Gemcitabine	2 (7.1)
Vinorelbine	3 (10.7)
Others	1 (3.6)

Table 5. First-line systemic treatment options of mTNBC patients.

	Regimens in the first-line treatment (n=59)
Capecitabine	16 (27.1)
Taxanes	29 (49.2)
Cisplatin/carboplatin	34 (57.6)
Gemcitabine	13 (22.0)
Vinorelbine	2 (3.4)
Anthracycline	2 (3.4)
Cyclophosphamide	3 (5.1)
Bevacizumab	4 (6.8)
Eribulin	2 (3.4)
PD1/PD-L1	8 (13.6)
ADC	5 (8.5)
PARP inhibitor	1 (1.7)
TKIs	3 (5.1)
Others	1 (1.7)

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Abbreviations

estrogen receptor, ER; ^{18}F-fluoroestradiol positron emission tomography/computed tomography, ^{18}F-FES PET/CT; metastatic triple-negative breast cancer, mTNBC; propensity score matching, PSM; immunohistochemistry, IHC; disease control rate, DCR; objective response rate, ORR; overall survival, OS; progression-free survival, PFS; androgen receptor, AR.

Conlcusions

- **Patients with functional ER loss defined by FES-PET exhibit worse outcomes than mTNBC.**
- **The ER loss group showed a significantly higher rate of androgen receptor pathway positivity.**

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