

Predictive and prognostic value of FES PET/CT for patients with recurrent or metastatic breast cancer treated with endocrine therapy plus cyclin-dependent kinase 4/6 inhibitors



Jeong H, Ryu J, Jeong JH, et al. *Eur J Nucl Med Mol Imaging*. 2025;52(6):2096-2106.

Objective

To evaluate the prognostic and predictive value of estrogen receptor (ER) status and heterogeneity determined by ¹⁸F-fluoroestradiol (FES) positron emission tomography/ computed tomography (PET/CT) in patients with ER-positive, human epidermal growth factor receptor 2 (HER2)–negative recurrent/metastatic breast cancer (BC) treated with cyclin-dependent kinase 4/6 (CDK4/6) inhibitor-based endocrine therapy (ET)

Study Design

Retrospective analysis of a prospective cohort from FES PET/CT postmarketing surveillance study

- Participants:



127
women

57
median age

81.9%
postmenopausal

CDK4/6 inhibitor-based ET

Aromatase inhibitors (AI)
75.6%
(n=96)

fulvestrant
24.4%
(n=31)

FES status

FES-positive
80.3%
(n=102)

FES-negative + Mixed
19.7%
(n=25)

- Mixed: 17.3% (n=22)
- All FES-negative: 2.4% (n=3)

Of those with lobular carcinomas:

FES-positive 12.7%

with FES-negative 28.0%

In patients with immunohistochemistry results available (n = 73), higher proportions of ER low-positive/negative and PR-negative results were found in the “with FES-negative” group.

- Exclusion criteria:

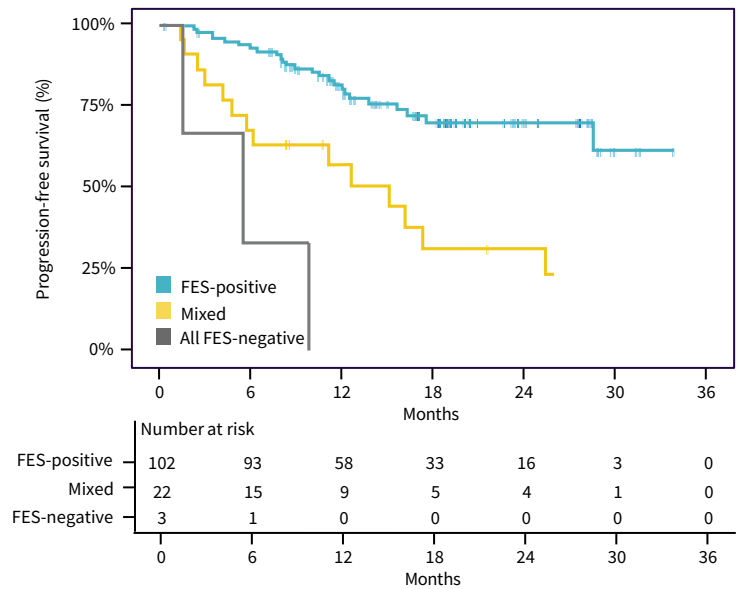


Patients with HER2-positive disease with concurrent malignancy who were lost to follow-up immediately after FES PET/CT, or without evaluable lesions on CT scans

Key Results

1. Progression-Free Survival (PFS)

(follow-up: 18.6 months [interquartile range, 13.1-25.2])

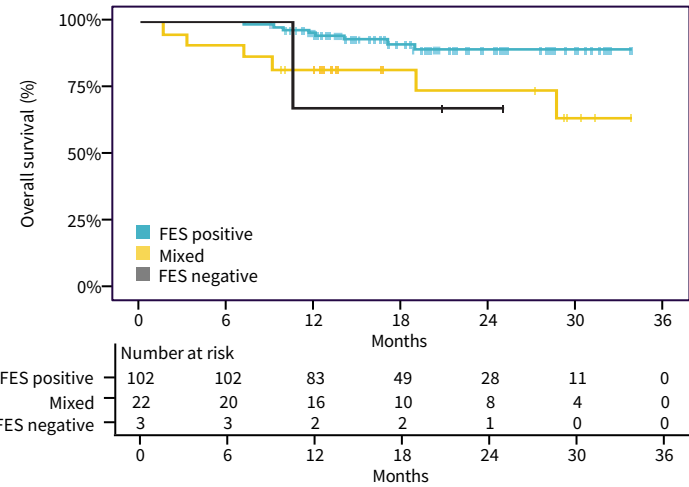


Population		PFS events	Median PFS (95% CI)	1-year PFS rate (95% CI)
Overall		43 patients; 15 deaths	28.4 mo (25.4-NE)	—
FES-positive		25/102 patients	Not reached (28.4-NE)	81.9% (72.5-88.4)
FES-negative + Mixed		18/25 patients	11.1 mo (5.6-17.3)	49.5% (28.0-67.8)
	Mixed	—	15.0 mo (4.8-25.4)	—
	All FES-negative	—	5.6 mo (1.6-NE)	—

CI, confidence interval; mo, months; NE, not estimated.

The hazard ratio for PFS was 3.9 (95% CI, 2.1–7.2) in the FES-negative + Mixed group (P<0.001)

2. Overall Survival (OS)



Population	Deaths	Median OS (95% CI)	1-year OS rate (95% CI)
Overall	—	Not reached (NE)	—
FES-positive	8/102 patients	Not reached (NE)	95.9% (89.4-98.4)
FES-negative + Mixed	7/25 patients	Not reached (19.0-NE)	79.6% (57.7-91.0)

CI, confidence interval; NE, not estimated; OS, overall survival.

The hazard ratio for OS was 3.7 (95% CI, 1.3–10.2) in the FES-negative + Mixed group ($P=0.008$)

3. Clinical Benefit Rate (CBR)

- Among all patients, the CBR of ET plus CDK4/6 inhibitors was greater in the FES-positive groups than in the FES-negative + Mixed group (91.2% vs 72.0%, $P=0.017$).
- Among the 87 patients with measurable disease, the CBR was also higher in the FES-positive groups than in the FES-negative + Mixed group (92.2% vs 69.6%, $P=0.013$).

4. Subgroup Analysis

- While on AI therapy, patients in the FES-negative + Mixed group had ~5× higher risk of progression compared with patients in FES-positive group ($P<0.001$).
- While on fulvestrant, median PFS for patients in FES-positive group was ~5-month longer than PFS for patients in the FES-negative + Mixed group, however this was not statistically significant ($P=0.104$).

Limitations

1. Single-center study with a population limited to East Asian ethnicity, reducing generalizability
2. Retrospective analysis of a prospective cohort; treatment decisions made by attending physicians without prospective interventions
3. Small sample sizes, especially in the subgroup analyses, limiting statistical power
4. Variability in conventional imaging modalities potentially influencing detection of FES-negative lesions
5. Visual analysis of FES uptake, potentially less reproducible than semi-quantitative thresholds
6. Limitations of FES PET/CT in assessing liver lesions and detecting other mechanisms of endocrine resistance

Considerations

- Further studies are needed to validate findings across diverse populations and assess the utility of FES PET/CT in predicting ET resistance.
- Exploration of alternative treatments, such as upfront chemotherapy, for patients with completely FES-negative lesions is warranted.



Clinical Implications
Large, prospective study from real-world clinical practice reported comparable predictive and prognostic impact of FES PET to that in previous studies.^{1,2}

- Approximately 20% of patients clinically indicated for ET plus CDK4/6 inhibitors had FES-negative lesions and significantly shorter PFS compared with those with all FES-positive lesions.
- ER heterogeneity is more common in invasive lobular carcinoma than in invasive ductal carcinoma.
- With a CBR of 72%, patients with FES-negative lesions derived clinically meaningful benefit from ET plus CDK4/6 inhibitors.

References
1. Liu C, et al. *Breast Cancer Res*. 2022;24:57.
2. Boers J, et al. *Eur J Cancer*. 2020;126:11–20.

CERIANTA™ (fluoroestradiol F18) injection is indicated for use with PET imaging of ER-positive lesions as an adjunct to biopsy in patients with recurrent or metastatic BC, with limitations including the need for biopsy confirmation and lack of utility for other receptors (eg, HER2, PR). The use of FES PET/CT to assess prognosis, predict treatment response, or guide therapy decisions has not been approved, and its safety and effectiveness for these uses have not been established. CERIANTA has no listed contraindications; warnings include risk of misdiagnosis and radiation exposure. For full prescribing information, visit https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212155s000lbl.pdf.

