BJMS
www.batnajms.net

Batna Journal of Medical Sciences 2026;13(6):xx
https://doi.org/10.48087/BJMS.2026.1306xx

ORIGINAL ARTICLE

First-Line Endocrine Therapy Effectiveness in Recurrent HR+/HER2− Metastatic Breast Cancer: A Comprehensive Retrospective Study in Eastern Algeria

Asma BOUDERSA[1], Nassima KOUADRI[1], Taha FILALI[2]

ABSTRACT

Background: Recurrent hormone receptor–positive (HR+), HER2-negative metastatic breast cancer remains a therapeutic challenge due to its biological heterogeneity and prior exposure to adjuvant endocrine therapy. Endocrine therapy continues to play a central role in the absence of visceral crisis. **Objectives:** To evaluate the effectiveness of first-line endocrine therapy in patients with recurrent HR+/HER2− metastatic breast cancer previously treated with adjuvant hormonal therapy, using median progression-free survival (mPFS) as the primary endpoint. **Methods:** This retrospective study was conducted in Eastern Algeria and included 45 patients with recurrent HR+/HER2− metastatic breast cancer. Patients were recruited between 2020 and 2023 and selected based on ECOG performance status ≤ 3, histologically confirmed invasive breast carcinoma with metastatic recurrence after adjuvant treatment, and positive hormone receptor status (ER+ and/or PR+). Hormone-naïve patients and those with visceral crisis requiring chemotherapy were excluded. All patients received first-line endocrine therapy in the metastatic setting. Progression-free survival was estimated using the Kaplan–Meier method. This study was conducted using patient medical records. All data were anonymized, and patient confidentiality was strictly maintained. **Results:** The mean age was 57.87 years, and 80% of patients were postmenopausal. Comorbidities were present in 42% of cases. Bone metastases were observed in 71% of patients, while 44.4% had visceral involvement; 66.7% presented with multiple metastatic sites. Aromatase inhibitors were administered in 55.6% of patients and anti-estrogens in 44.5%. The median PFS was 12.97 months (95% CI: 7.93–18.03). The response rate at 6 months was 33.4%, including two complete responses. Tumor response evaluation was performed according to the RECIST 1.1 criteria. Median overall survival was 26.0 months. Skeletal-related events occurred in 33.3% of patients. **Conclusion:** First-line endocrine therapy demonstrates meaningful clinical activity in recurrent HR+/HER2− metastatic breast cancer, particularly in patients with bone-predominant disease and strong hormone receptor expression. Despite the advent of CDK4/6 inhibitors, endocrine monotherapy remains a valid option in selected patients.

Keywords: Breast cancer, luminal, metastatic, endocrine therapy, relapse.

1. Faculty of medicine of Annaba, Algeria
2. Faculty of medicine Constantine, Algeria

Received: 22 Jan 2026
Accepted: 01 Mar 2026

Correspondance to: Asma BOUDERSA
E-mail: as.onco@yahoo.fr

List of abbreviations:
mPFS: median of progression free survival
HR: Hormone receptor
HER2: Human epithelial growth factor receptor2
IDC: Invasive ductal carcinoma
ER; Estrogen receptor
PR: Progesterone receptor
SBR: Scarff Bloom Richardson
CDK4/6: Cyclinedependant kinase
OS: Overall survival

1. INTRODUCTION

Recurrent metastatic breast cancer (MBC) is a heterogeneous disease at clinical, histopathological, and molecular levels, which partly explains its variable prognosis and frequent resistance to systemic therapies. Hormone receptor–positive (HR+), HER2-negative breast

cancer represents the most frequent subtype, and endocrine therapy (ET) remains a cornerstone of treatment in the absence of a visceral crisis. **[1, 2]**

This study aimed to evaluate the effectiveness of first-line endocrine therapy in patients with recurrent HR+/HER2− metastatic breast cancer previously exposed to adjuvant hormonal treatment. The primary endpoint was median progression-free survival (mPFS).

2. PATIENTS AND METHODS

This study was conducted in Eastern Algeria and included 45 patients with recurrent HR+/HER2− metastatic breast cancer. Data were collected retrospectively from medical records, with patient recruitment performed between 2020 and 2023. We included women aged over 18 years with an Eastern Cooperative Oncology Group performance status (ECOG PS) ≤ 3, diagnosed with histologically confirmed invasive breast carcinoma with metastatic recurrence after adjuvant treatment, documented histologically and/or radiologically, and with positive hormone receptor status (ER+ and/or PR+) and HER2-negative disease. We excluded hormone-naïve patients and those presenting with a visceral crisis that required chemotherapy. All patients received first-line endocrine therapy in the metastatic setting. Progression-free survival was estimated using the Kaplan–Meier method. This study was conducted using patient medical records. All data were anonymized, and patient confidentiality was strictly maintained.

3. RESULTS

A total of 45 patients with recurrent HR-positive, HER2-negative metastatic breast cancer were included. The mean age was 57.87 years, and 80% of patients were postmenopausal. A family history of cancer was reported in 24% of cases. Comorbidities were present in 42% of patients. Visceral metastases were observed in 44.4% of patients, while 66.7% presented with multiple metastatic sites. Bone-related events occurred in 33.3% of cases.

Histologically, invasive ductal carcinoma (IDC) was the predominant subtype, accounting for 80% of tumors, followed by invasive lobular carcinoma (ILC) in 15.6%. Most tumors were of intermediate or high grade, with Scarff–Bloom–Richardson (SBR) grade II in 78% and grade III in 14.6% of cases. A Ki-67 index greater than 20% was observed in 37.6% of tumors. Strong hormone receptor expression was frequent, with estrogen receptor (ER) positivity greater than 60% in 62.5% of patients and progesterone receptor (PR) positivity greater than 60% in 57.2%. It is a luminal A type in 53% of cases versus 47% for group B **(Table 1).** Regarding first-line endocrine treatment, 55.6% of patients received aromatase inhibitors, while 44.5% were treated with anti-estrogens. LHRH analogues were used in 4% of cases.

The median progression-free survival (mPFS) under first-line endocrine therapy was 12.97 months. The response rate at 6 months was 33.4% (Figure 1)**.** Tumor response was assessed according to RECIST 1.1 criteria. Complete response (CR), observed in 4.4% of patients, was defined as the disappearance of all target lesions with normalization of pathological lymph nodes (<10 mm in short axis) and no appearance of new lesions. Partial response (PR), observed in 13.3%, was defined as a ≥30% decrease in the sum of diameters of target lesions compared with baseline, with no new lesions or disease progression. Stable disease (SD), observed in 15.6%, was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, without new lesions. Progressive disease (PD), observed in 64.4%, was defined as a ≥20% increase in the sum of diameters of target lesions (with an absolute increase of at least 5 mm) or the appearance of new lesions. In the second-line setting, 37.8% of patients received endocrine therapy, 22.2% received chemotherapy, and 40% did not receive further treatment [3].

4. DISCUSSION

This study describes real-world outcomes of patients with recurrent hormone receptor–positive, HER2-negative metastatic breast cancer treated with first-line endocrine therapy. The mean age of 57.87 years and the predominance of postmenopausal women (80%) are consistent with previously reported populations most frequently eligible for hormonal treatment. Indeed, hormone receptor–positive/HER2-negative disease is the most common biological subtype of breast cancer and is predominantly diagnosed in older and postmenopausal women, who represent the main candidates for endocrine-based therapies.

These findings are consistent with international evidence and consensus guidelines supporting endocrine therapy as the standard first-line treatment in the absence of a visceral crisis. The ESO–ESMO Advanced Breast Cancer (ABC 5) guidelines clearly recommend endocrine therapy as the preferred initial approach for postmenopausal patients with hormone receptor–positive, HER2-negative metastatic disease, particularly in clinically stable patients without rapidly progressive or life-threatening visceral involvement **[4].**

Table 1. Anamnestic, clinico-histological, and therapeutic data of the hormonal metastatic recurrence group.

		BREAST M+ HORMONO RECURRENCE N : 45
Age (year)		57.87
Menopaused (%)		80%
Family history (%)		24%
Comorbidities		42%
Visceral metastasis		44.4%
M+ Multiple		66.7%
Histology	**IDC**	80%
	ILC	15.6%
SBR	**2**	78%
	3	14.6%
Ki-67> 20%		37.6%
E R(+)> 60%		62.5 %
PR (+)> 60%		57.2%
Type	**AI**	55.6%
Of HT	**AO**	44.5%
	AI+AO	/
	A-LHRH	4%
Median of PFS		**12.97 months**
Response rate at 6 months		**33.4%**
Evolution	**RC**	4.4%
	RP	13.3%
	SD	15.6%
	PD	64.4%
TRT 2 L	**HT**	37.8 %
	CT	22 .2 %
	NFT	40%
Bone event		33.3%

M+: metastasis, ER : Estrogen receptor,PR :Progesterone receptor, HT :hormone therapy, SBR: grade Scarff Bloom Richardson, TRT 2L: Treatment of second ligne. NFT: no further treatment; IDC: Invasive ductal carcinoma; ILC: Invasive lobular carcinoma.

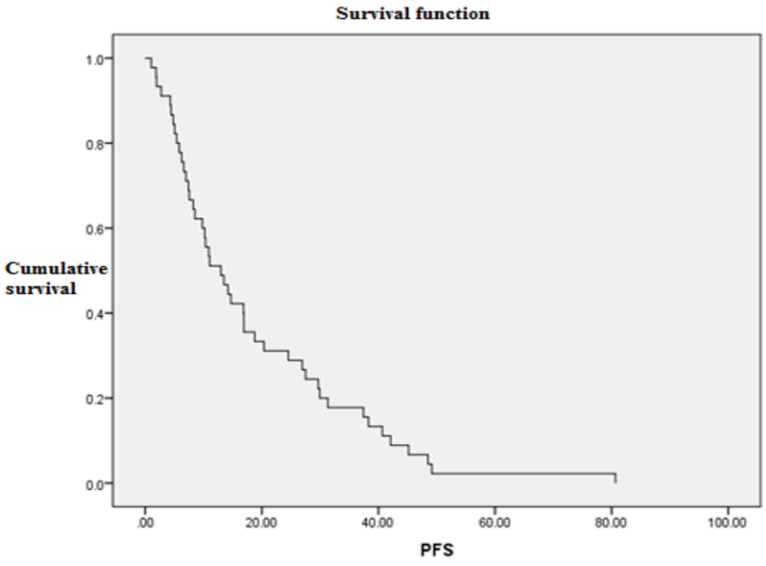


Figure 1. PFS curve of first-line HT in the recurrence group after hormonal therapy.

Similarly, evidence from real-world and clinical comparative studies has demonstrated that first-line endocrine therapy is commonly used in postmenopausal patients and is associated with outcomes comparable to chemotherapy in appropriately selected patients. Song et al. reported that endocrine therapy is frequently chosen in this population due to its favorable toxicity profile and clinical effectiveness, supporting its role as a standard first-line option in routine practice **[5].** In addition, Shimoi et al., in a systematic review and meta-analysis, confirmed the relevance of first-line endocrine therapy in postmenopausal patients with hormone receptor–positive, HER2-negative metastatic breast cancer, highlighting its efficacy and tolerability in this setting **[6].**

Overall, these data reinforce that the demographic characteristics observed in our cohort reflect the typical population eligible for endocrine-based treatment strategies. They also underline the alignment of real-world practice with international recommendations favoring endocrine therapy as the backbone of first-line treatment in postmenopausal patients with hormone receptor–positive, HER2-negative metastatic breast cancer**. [4-6]**

Comorbidities were present in nearly half of the patients (42%), a factor that likely influenced the preference for first-line endocrine therapy due to its favorable safety profile compared with chemotherapy, particularly in medically fragile patients. Real-world evidence and international guidelines support endocrine therapy as the standard first-line treatment for hormone receptor–positive, HER2-negative metastatic breast cancer in the absence of a visceral crisis. The relatively high proportion of bone involvement reflects the natural history of luminal breast cancer, which is characterized by a predominance of skeletal metastases. Although chemotherapy has historically been overused in some settings, real-world data from China indicate a gradual increase in the use of endocrine therapy and a persistent proportion of patients receiving chemotherapy despite guideline recommendations, highlighting the need for improved adherence to clinical guidelines[7].

Visceral metastases were present in 44.4% of cases, indicating that endocrine therapy was used even in patients with visceral involvement, likely in the absence of a visceral crisis. This observation is consistent with current international recommendations, which support the use of endocrine therapy as first-line treatment in patients with hormone receptor–positive, HER2-negative metastatic breast cancer, provided that the disease is not rapidly progressive or immediately life-threatening. In such settings, the presence of visceral metastases alone does not preclude the use of endocrine therapy, particularly when the clinical course remains indolent. **[4, 8]**.

The predominance of invasive ductal carcinoma in our cohort reflects the most common histological subtype observed in breast cancer. Furthermore, the high proportion of tumors with SBR grade II and III suggests relatively aggressive tumor biology, which may be associated with an increased risk of recurrence and metastatic spread. However, it is important to note that even within this context, hormone receptor–positive tumors often retain a degree of endocrine sensitivity, supporting the continued role of endocrine therapy in appropriately selected patients.

Taken together, these findings highlight the heterogeneity of metastatic breast cancer and emphasize that treatment decisions should not rely solely on the presence of visceral disease or histological grade, but rather on a comprehensive assessment including disease kinetics, symptom burden, and evidence of endocrine responsiveness**. [4, 9]**

Strong hormone receptor expression was common, with more than 60% ER and PR positivity in the majority of patients, supporting the biological rationale for endocrine sensitivity. The use of aromatase inhibitors in more than half of the patients reflects standard practice in postmenopausal women, while anti-estrogens were mainly used in selected cases. **[10]**

The median progression-free survival (PFS) of 12.97 months demonstrates a clinically meaningful benefit of endocrine therapy in this recurrent metastatic setting. Despite prior exposure to adjuvant hormonal treatment, disease control was achieved in a subset of patients, as reflected by the observed response and stable disease rates. However, disease progression remained frequent, occurring in more than 60% of cases, highlighting the limitations of endocrine monotherapy in this population. These findings are consistent with previous studies showing that while endocrine therapy remains effective in hormone receptor–positive metastatic breast cancer, resistance eventually develops in a significant proportion of patients **[11]**. Moreover, the addition of targeted agents such as CDK4/6 inhibitors has been shown to significantly improve progression-free survival compared with endocrine therapy alone, underscoring the evolving standard of care **[12–14]**

A substantial proportion of patients continued to receive endocrine therapy in the second-line setting, confirming its ongoing role in disease management. The occurrence of bone-related events in one-third of patients emphasizes the need for optimal bone-targeted supportive care. **[15]**

Limitations

This study has several limitations inherent to its retrospective design. The relatively small sample size (n = 45) limited statistical power and precluded the identification of robust prognostic or predictive factors. Missing or incomplete data in medical records, particularly regarding tumor characteristics and long-term follow-up, may have influenced survival estimates. No formal sample size calculation was performed, as this work represents a secondary exploratory analysis derived from a prospective cohort evaluating first-line hormone therapy in metastatic breast cancer **[16, 17].** The aim of this analysis was to compare outcomes between hormone-naïve and hormonally pre-treated (recurrent) patients rather than to test a pre-specified primary hypothesis requiring formal power calculation. Data collection was further affected by the COVID-19 pandemic, which limited access to medical records and constrained data retrieval, thereby contributing to the restricted sample size. The absence of a centralized computerized database may have introduced heterogeneity in data collection and potential information bias. In addition, treatment strategies were not standardized and reflected real-world clinical practice, which may limit the generalizability of the findings. Finally, the lack of a comparative control group precluded direct comparison with other therapeutic strategies.

5. CONCLUSION

In this real-world retrospective study, first-line endocrine therapy demonstrated meaningful clinical activity in patients with recurrent HR-positive, HER2-negative metastatic breast cancer previously exposed to adjuvant hormonal treatment. A median progression-free survival of 12.97 months was observed, particularly in patients with strong hormone receptor expression and a high prevalence of bone involvement. Despite these encouraging results, disease progression remained frequent, highlighting the limitations of endocrine monotherapy in this setting. The introduction of CDK4/6 inhibitors has substantially changed the therapeutic landscape, and endocrine monotherapy should now be reserved for carefully selected patients, particularly those with contraindications to combination therapy or significant comorbidities. Further prospective studies with larger cohorts and standardized data collection are needed to better define the optimal sequencing of endocrine therapies and to identify predictive factors of response in recurrent luminal metastatic breast cancer.

Competing interests: The authors declare that they have no competing interest.

Funding: This research received no external funding.

REFERENCES

1. Ferro, A., Campora, M., Caldara, A., De Lisi, D., Lorenzi, M., Monteverdi, S., Mihai, R., Bisio, A., Dipasquale, M., Caffo, O., & Ciribilli, Y. (2024). Novel Treatment Strategies for Hormone Receptor (HR)-Positive, HER2-Negative Metastatic Breast Cancer. *Journal of Clinical Medicine*, *13*(12), 3611. https://doi.org/10.3390/jcm13123611
2. Singareeka Raghavendra, A., Damodaran, S., Barcenas, C. H., Fuqua, S. A., Layman, R. M., & Tripathy, D. (2026). Personalizing therapies over the course of hormone receptor-positive/HER2-negative metastatic breast cancer. *CA: a cancer journal for clinicians*, *76*(1), e70055. https://doi.org/10.3322/caac.7005
3. Eisenhauer, E. A., Therasse, P., Bogaerts, J., Schwartz, L. H., Sargent, D., Ford, R., Dancey, J., Arbuck, S., Gwyther, S., Mooney, M., Rubinstein, L., Shankar, L., Dodd, L., Kaplan, R., Lacombe, D., & Verweij, J. (2009). New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). European journal of cancer (Oxford, England : 1990), 45(2), 228–247. https://doi.org/10.1016/j.ejca.2008.10.026
4. Cardoso, F., Paluch-Shimon, S., Senkus, E., Curigliano, G., Aapro, M. S., André, F., Barrios, C. H., Bergh, J., Bhattacharyya, G. S., Biganzoli, L., Boyle, F., Cardoso, M. J., Carey, L. A., Cortés, J., El Saghir, N. S., Elzayat, M., Eniu, A., Fallowfield, L., Francis, P. A., Gelmon, K., … Winer, E. P. (2020). 5th ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 5). Annals of oncology : official journal of the European Society for Medical Oncology, 31(12), 1623–1649. https://doi.org/10.1016/j.annonc.2020.09.01
5. Song Y, Hao Y, Macalalad AR, Lin PL, Signorovitch JE, Wu EQ. Clinical Outcomes with First-line Endocrine Therapy or Chemotherapy in Postmenopausal HR+/HER2- Metastatic Breast Cancer. Breast Cancer (Auckl). 2015 Sep 3;9:67-72. doi: 10.4137/BCBCR.S30771. PMID: 26380551; PMCID: PMC4560455.
6. Shimoi, T., Sagara, Y., Hara, F., Toyama, T., & Iwata, H. (2020). First-line endocrine therapy for postmenopausal patients with hormone receptor-positive, HER2-negative metastatic breast cancer: a systematic review and meta-analysis. Breast cancer (Tokyo, Japan), 27(3), 340–346. https://doi.org/10.1007/s12282-020-01054-7
7. Yuan, Y., Zhang, S., Yan, M., Yin, Y., Song, Y., & Jiang, Z. (2021). Chemotherapy or endocrine therapy, first-line treatment for patients with hormone receptor-positive HER2-negative metastatic breast cancer in China: a real-world study. Annals of translational medicine, 9(10), 831. https://doi.org/10.21037/atm-20-8252
8. Partridge, A. H., Rumble, R. B., Carey, L. A., Come, S. E., Davidson, N. E., Di Leo, A., Gralow, J., Hortobagyi, G. N., Moy, B., Yee, D., Brundage, S. B., Danso, M. A., Wilcox, M., & Smith, I. E. (2014). Chemotherapy and targeted therapy for women with human epidermal growth factor receptor 2-negative (or unknown) advanced breast cancer: American Society of Clinical Oncology Clinical Practice Guideline. Journal of clinical oncology : official journal of the American Society of Clinical Oncology, 32(29), 3307–3329. https://doi.org/10.1200/JCO.2014.56.7479.
9. Gradishar, W. J., Anderson, B. O., Abraham, J., Aft, R., Agnese, D., Allison, K. H., Blair, S. L., Burstein, H. J., Dang, C., Elias, A. D., Giordano, S. H., Goetz, M. P., Goldstein, L. J., Isakoff, S. J., Krishnamurthy, J., Lyons, J., Marcom, P. K., Matro, J., Mayer, I. A., Moran, M. S., … Kumar, R. (2020). Breast Cancer, Version 3.2020,

NCCN Clinical Practice Guidelines in Oncology. Journal of the National Comprehensive Cancer Network : JNCCN, 18(4), 452–478. https://doi.org/10.6004/jnccn.2020.0016

10. Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Davies, C., Godwin, J., Gray, R., Clarke, M., Cutter, D., Darby, S., McGale, P., Pan, H. C., Taylor, C., Wang, Y. C., Dowsett, M., Ingle, J., & Peto, R. (2011). Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. Lancet (London, England), 378(9793), 771–784. https://doi.org/10.1016/S0140-6736(11)60993-8.
11. Rugo, H. S., Rumble, R. B., Macrae, E., Barton, D. L., Connolly, H. K., Dickler, M. N., Fallowfield, L., Fowble, B., Ingle, J. N., Jahanzeb, M., Johnston, S. R., Korde, L. A., Khatcheressian, J. L., Mehta, R. S., Muss, H. B., & Burstein, H. J. (2016). Endocrine Therapy for Hormone Receptor-Positive Metastatic Breast Cancer: American Society of Clinical Oncology Guideline. Journal of clinical oncology : official journal of the American Society of Clinical Oncology, 34(25), 3069–3103. https://doi.org/10.1200/JCO.2016.67.1487
12. Turner, N. C., Ro, J., André, F., Loi, S., Verma, S., Iwata, H., Harbeck, N., Loibl, S., Huang Bartlett, C., Zhang, K., Giorgetti, C., Randolph, S., Koehler, M., Cristofanilli, M., & PALOMA3 Study Group (2015). Palbociclib in Hormone-Receptor-Positive Advanced Breast Cancer. The New England journal of medicine, 373(3), 209–219. https://doi.org/10.1056/NEJMoa1505270
13. Sledge, G. W., Jr, Toi, M., Neven, P., Sohn, J., Inoue, K., Pivot, X., Burdaeva, O., Okera, M., Masuda, N., Kaufman, P. A., Koh, H., Grischke, E. M., Frenzel, M., Lin, Y., Barriga, S., Smith, I. C., Bourayou, N., & Llombart-Cussac, A. (2017). MONARCH 2: Abemaciclib in Combination With Fulvestrant in Women With HR+/HER2- Advanced Breast Cancer Who Had Progressed While Receiving Endocrine Therapy. Journal of clinical oncology : official journal of the American Society of Clinical Oncology, 35(25), 2875–2884. https://doi.org/10.1200/JCO.2017.73.7585.
14. Hortobagyi, G. N., Stemmer, S. M., Burris, H. A., Yap, Y. S., Sonke, G. S., Paluch-Shimon, S., Campone, M., Blackwell, K. L., André, F., Winer, E. P., Janni, W., Verma, S., Conte, P., Arteaga, C. L., Cameron, D. A., Petrakova, K., Hart, L. L., Villanueva, C., Chan, A., Jakobsen, E., … O'Shaughnessy, J. (2016). Ribociclib as First-Line Therapy for HR-Positive, Advanced Breast Cancer. The New England journal of medicine, 375(18), 1738–1748. https://doi.org/10.1056/NEJMoa1609709
15. Le Saux O, Lardy-Cleaud A, Frank S, Debled M, Cottu PH, Pistilli B, et al. Assessment of the efficacy of successive endocrine therapies in hormone receptor-positive and HER2-negative metastaticbreast cancer: a real-life multicentre national study. Eur J Cancer OxfEngl 1990. sept 2019;118:131-41.
16. Boudersa A et al. The Median of Progression free survival in Patients with HR+/HER2− Metastatic Breast Cancer Treated with Initial Endocrine Therapy in Eastern Algeria. A prospective study. Batna J Med Sci 2025; 12(2): 187-195
17. l'hormonothérapie de première ligne dans le cancer du sein métastatique rh+/ her2- entre recommanadations et pratiques. https://dspace.univ-annaba.dz//handle/123456789/3918.