BJMS BATNA JOURNAL OF MEDICAL SCIENCES
www.batnajms.net

BATNA JOURNAL OF MEDICAL SCIENCES
2024, VOL. 11, NO. 4, 442–446
DOI: 10.48087/BJMSoa.2024.11407

ORIGINAL ARTICLE

OPEN ACCESS

Evaluation of First-Line Endocrine Therapy for HR+/HER2- Metastatic Breast Cancer: Efficacy, Tolerance and Prescribing Practices. A Prospective and Observational study

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

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

ABSTRACT

Introduction: Endocrine therapy is commonly employed for MBC (Metastatic Breast Cancer) patients due to its efficacy in modulating hormone receptors and its generally favorable side effect profile. This study aims to evaluate the effectiveness and tolerability of first-line endocrine therapy in HR+(Hormone receptor)/HER2-(Human epithelial growth factor receptor) metastatic breast cancer patients, to investigate differences among various endocrine therapies, and examine changes in prescribing practices influenced by evolving clinical guidelines. **Methods:** We conducted a multicenter, observational, prospective study involving 100 women aged over 18 years with de novo HR+, HER2- MBC. Data were collected between 2020 and 2023. The primary objective was to assess the ORR (Objective Response Rate) at 6 months under first-line endocrine therapy. Secondary objectives included evaluating the influence of types of endocrine therapy on the ORR, the evolution of the response at 2 years, clinical efficacy, and tolerability. **Results:** At 6 months, the ORR was 38%, with 3 complete responses (CR). No significant difference in ORR was observed between aromatase inhibitors and Faslodex (p=0.439). The clinical benefit rate was 80%. 84% of patients reporting mild to moderate adverse effects. **Discussion:** A first-line endocrine therapy for HR+/HER2- MBC offers substantial clinical benefit rate with an 80%, and manageable side effects. Despite a lower ORR, the therapy effectively controls disease progression and preserves quality of life. The results support the continued use of endocrine therapy while emphasizing the importance of managing adverse effects. Initial hesitations among practitioners were due to concerns about its efficacy. **Conclusion:** Endocrine therapy provides significant clinical benefits and maintains patient quality of life.

ARTICLE HISTORY
Received 20 Oct 2024
Accepted 22 Nov 2024

KEYWORDS
Endocrine therapy, first line, metastatic breast cancer, hormone receptor positive

CORRESPONDING AUTHOR
Asma BOUDERSA
as.onco@yahoo.fr

1. INTRODUCTION

Metastatic breast cancer, in particular the hormone receptor-positive (RH+) subtype, poses significant challenges for therapeutic management. First-line hormone therapy is commonly used to treat these patients because of its effectiveness in modulating hormone receptors and its generally favorable tolerance profile compared to chemotherapy. However, the response to treatment can vary significantly depending on the individual characteristics of the patients and the type of hormone therapy administered. This study was designed to evaluate the efficacy and safety of first-line hormone therapy in patients with RH+/HER2-metastatic breast cancer, as well as to explore the potential differences between the various types of hormone therapy available. The main objective of this research is to measure the objective response rate at 6 months

To cite the article: Boudersa A et al. Evaluation of First-Line Endocrine Therapy for HR+/HER2- Metastatic Breast Cancer: Efficacy, Tolerance and Prescribing Practices. A Prospective and Observational study. Batna J Med Sci 2024; 11(4): 482-486

in patients receiving first-line hormone therapy for RH+/HER2- metastatic breast cancer. The secondary objectives include the analysis of the influence of the type of hormone therapy on the response to treatment, the evolution of the response after 2 years, the overall clinical effectiveness, and the tolerance to the treatments administered. The study also aims to evaluate the side effects and the overall impact of these treatments on the patients' quality of life.

2. PATIENTS AND METHODS

Our bibliographic research was carried out from PubMed using the following Mesh terms: endocrine therapy, first line, metastatic breast cancer, hormone receptor positive. Regarding the management of bibliographic references, we used the "Zotero" software. We conducted an observational, prospective and multicenter, non-interventional study on a sample of 100 patients. We included women over the age of 18, with a PS less than or equal to 3, who are suffering from histologically proven infiltrative breast cancer, metastatic de novo, with ER+ (Estrogen receptor) and/or PR+ (Progesterone Receptor), HER2- .The primary objective is to evaluate the objective response rate at 6 months, under first-line hormone therapy, in patients with RH+/HER2- metastatic breast cancer. The secondary objectives are to investigate the influence of the type of hormone therapy on the response rate, the evolution of the response at 2 years, clinical efficacy, and tolerance. For statistical analyses, group comparisons are carried out for quantitative variables by the nonparametric Wilcoxon test. For qualitative variables, the Chi2 test or the Fisher test, when the numbers justify it, are used. A $p < 0.05$ in bilateral testing is considered significant.

In this study, the anonymity of the patients is respected, and the study agrees with the Helsinki declaration.

3. RESULTS

Table 1. Six-month Objective response rate (ORR).

	N	%
Not specified	6	6.0
PD	14	14.0
CR	3	3.0
PR	35	35.0
SD	42	42.0
Total	100	100.0

N : effective, PD : progression, CR : Complete response, PR : partial response, SD : stability

The study included 100 patients followed in one of the oncology departments located in Eastern Algeria previously chosen as investigating centers, in a period between 2020 and 2023, all concerned by the analysis of admission and therapeutic data. These are patients with de Novo metastatic breast cancer of the luminal non-HER2 type. The average age is 62.88 years. These are postmenopausal women in 85% of cases.

In our series, the objective response rate at 6 months is 38**%**, including 3 complete answers and 35 with a partial answer**.** Fourteen patients (14) who have progressed within 6 months of the start of treatment thus determining the group which presents a primary hormone resistance. In six patients, the evaluation was not carried out either by death **(**2 patients) or because the patients were lost to sight before the first evaluation (4 patients).

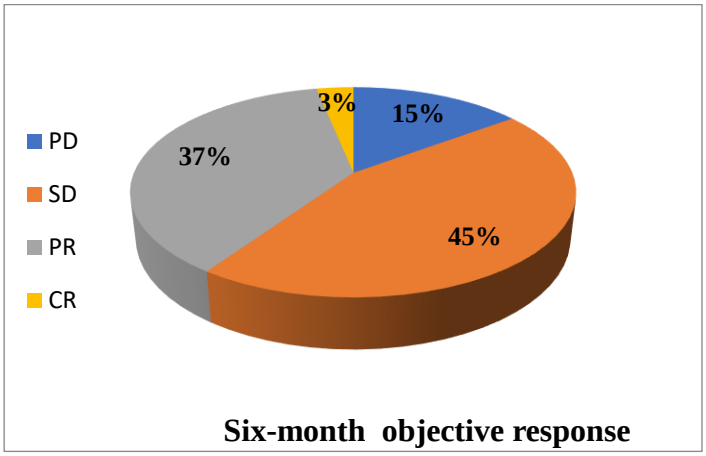

Figure 1. Six-month response.

Depending on the type of first-line hormone therapy, there is no significant difference between anti-aromatases and Faslodex with regard to the objective response at 6 months (p=0.439).

Table 2. OR according to the types of hormone therapy.

		OR_6M				Total
		CR	PR	SD	PD	
Faslodex	number	8_a	16_a	19_a	1_a	44
	%	61.5%	47.1%	63.3%	100.0%	56.4%
AI	number	5_a	18_a	11_a	0_a	34
	%	38.5%	52.9%	36.7%	0.0%	43.6%
Total	number	13	34	30	1	78
	%	100.0%	100.0%	100.0%	100.0%	100.0%

OR_6M: objective response at 6 months, AI: aromatase inhibitor

To cite the article: Boudersa A et al. Evaluation of First-Line Endocrine Therapy for HR+/HER2- Metastatic Breast Cancer: Efficacy, Tolerance and Prescribing Practices. A Prospective and Observational study. Batna J Med Sci 2024; 11(4): 482-486

The clinical benefit rate defines as the sum of complete responses, partial responses, and stabilization of the disease ≥ 24 weeks) (1). The clinical benefit rate within 06 months of hormone therapy treatment is 80% of the patients in our series. Most patients reported an improvement in their general condition, a regression of pain or even a decrease in the use of painkillers.

Table 3. The evolution under hormonal therapy: response to 2 years.

Valid	NP	6	6.0	6.0
	PD	52	52.0	52.0
	CR	4	4.0	4.0
	PR	16	16.0	16.0
	SD	22	22.0	22.0
	Total	100	100.0	100.0

NP: not precise, PD: progression, CR: Complete response, PR: partial response, SD: stability

During the follow-up period of the patients, 52 of them progressed, 22 remained stable, 16 partially responded to the treatment while 4 women presented a complete response. Regarding the tolerance to treatments, it is difficult to specify the side effects related to each hormonal treatment, Eighty-four percent (84%) of patients reported moderate or minimal adverse reactions, of which hot flashes represent the main symptom. Three patients on Tamoxifene have developed cysts or fibroids, but none is complicated or requires surgery. More than 80% of patients on AI (anti-aromatases) have received calcium and vitamin D3 supplementation at least once; the majority of them take bisphosphonates as a preventive measure every 03 to 06 months according to BMD (Bone Mineral Density test) data. More than 60% reported the notion of arthralgia or myalgia during treatment. No interruption of treatment related to the poor tolerance of one of the hormone therapy molecules is recorded. For the study of the impact of this HT (Hormone Therapy) on the quality of life of patients, we noticed that at the beginning of recruitment in 2020, and before starting treatment, following the fact of proposing hormone therapy, the majority of patients transmitted their fears about its effectiveness compared to chemotherapy. While this idea has been attenuated over the subsequent recruitments. The majority of our patients have reported that the treatment with hormone therapy has not impacted their daily lives, despite the occurrence of certain adverse effects related to the blocking of female hormones (estrogen and progesterone) known for their beneficial role for women's health and well-being. Mood disorders, fatigue, anxiety, sleep disturbance represent the most remarkable effects, but these signs are considered acceptable by patients. Indeed, this hormone therapy has made it possible to preserve the quality of life according to the patients but also according to the analysis of the data on the patients' files.

Four medical oncology departments located in eastern Algeria have been chosen as investigating centers, and several oncologists have been asked to participate in this work whose professional experience varies from 4 to more than 30 years. And since it is an observational study, the choice of treatment of which is left completely to the preferences of the practitioner, we noticed during the first year a reluctance to give hormone therapy especially by young oncologists who have less than 05 years of experience. We noticed during the two years after that the prescription habits changed markedly in favor of hormone therapy.

4. DISCUSSION

The average radiological response at 6 months is 38%. At the time of the analysis of the results, the average radiological response in this series reached 20% at 2 years, If we compare it with the data from the literature, this response rate is lower than that of Faslodex (46.1%) and Anastrozole (44.9%) in the Falcon study (2). this can be explained by the heterogeneity and diversity of the first-line treatment, which means that these several molecules do not have the same response rate, and therefore, it also has an impact on the median of PFS (Progression Free Survival), not to mention the selective nature of the Falcon study population. The clinical benefit rate reaches 80% within 06 months of treatment with hormone therapy. This reflects that the majority of our study population is hormone-sensitive. These results also show the effectiveness of hormone therapy in the control of metastatic breast disease of the non-HER2 luminal type. Most of the women interviewed showed a clinical improvement after two months of treatment: an improvement in their general condition, a regression of pain or even a decrease in the use of painkillers. It is difficult to specify the side effects related to each hormonal treatment, many mother molecules have been withdrawn; other brands have occupied the market, with a fluctuation in availability. The analysis of the tolerance data showed the absence of serious adverse reactions on the 100 patients studied. This reflects the good tolerability of hormone therapy. Hot flashes represent the main adverse effect which is consistent with the literature data. Its vasomotor effects have been the subject of several researches in order to limit their repercussions on the quality of life of the patients and to increase the adherence to the treatment (3). The presence of gynecological hemorrhages, cysts or fibroids following estrogen deprivation is relatively common (4) .We noticed the absence of a special dedicated consultation for the screening of these abnormalities for patients on anti-estrogens. Consultations are not systematic (on request if necessary). This lack of coordination of Onco-

To cite the article: Boudersa A et al. Evaluation of First-Line Endocrine Therapy for HR+/HER2- Metastatic Breast Cancer: Efficacy, Tolerance and Prescribing Practices. A Prospective and Observational study. Batna J Med Sci 2024; 11(4): 482-486

Gynecology services means that patients are scattered between the two sectors, public and private, according to their wishes and their financial power without there being a well-defined scheme to better take care of their patients. Some patients on anti-aromatases complain of arthralgia and myalgia known as classic complications of anti-aromatases. (5), (6) We have noticed an awareness on the part of practitioners who have developed the reflex to request bone densitometry before each prescription of anti-aromatases, but also have a tendency to often supplement patients with calcium and vitamin D3, as well as the use of bisphosphonates as a preventive measure every 06 months. No interruption of treatment related to the poor tolerance of one of the hormone therapy molecules is recorded. This is consistent with the literature; hormone therapy is a well-tolerated treatment by comparing its effects with those of chemotherapy, which is responsible for several acute complications that can sometimes be threatening. Awareness-raising and therapeutic education of patients seems to be an essential factor that contributes to the best management of adverse reactions.

Practitioners play a crucial role in disseminating information to patients about the potential risks of each therapy. We have noticed that the idea of the inferiority of hormone therapy compared to chemotherapy is less and less mentioned by patients, on the contrary some of them ask for another alternative less toxic than chemotherapy in order to preserve a good quality of life. During the diagnostic announcement, the fact that the oncologist is in front of a case of luminal metastatic cancer, it became obvious that the proposal of first-line hormone therapy is currently the most common option. Awareness-raising and therapeutic education have played a crucial role in this stage, such as advising on taking medications at night to reduce vasomotor effects during the morning, adapted physical activity or even taking medications in parallel.

Despite recent studies that speak of the alteration of the quality of life, especially cognitive, of patients undergoing hormone therapy, (7) in real life, patients show their satisfaction with not having acute complications of chemotherapy, especially vomiting, nausea, hair loss and hematological toxicities. These patients often keep their autonomy. Indeed, this hormone therapy has made it possible to preserve the physical quality of life according to the patients but also according to the analysis of the data on the patients' files. This positive feedback from patients and the sufficient hindsight with this hormone therapy whether on the ground or with the publications of the results of recent studies that have upset the practice; have encouraged practitioners to recommend it without fear.

After discussion with the practitioners, the main reason why they avoid giving hormone therapy is the fear of not being as effective as chemotherapy, especially in cases of visceral metastases or in young women. On the other hand, the inability to convince these metastatic patients of the effectiveness of hormone therapy for fear of linking the therapeutic results, in case of failure, to the wrong therapeutic choice of the attending physician. The lack of experience among young oncologists also seems to have influenced their therapeutic choices. We noticed during the two years after that the prescribing habits changed markedly in favor of hormone therapy. The clear and clear recommendations of learned societies on the subject, the CME (continuing medical education) and educational days as well as personal solicitation by telephone calls or face-to-face participated in this remarkable change in prescribing habits. What is remarkable in our study is that, after solicitation, these same young practitioners seem to be the most adherent to the new recommendations, which shows the impact of continuing education and awareness in our medical practice. By analyzing our anamnestic, clinical-histological and therapeutic data, we can extract certain criteria for the choice of hormone therapy by our practitioners. Indeed, they tend to put hormone therapy in elderly, postmenopausal patients, who present comorbidities, to avoid the toxicity linked to chemotherapy in this fragile population, and they chose anti aromatase over Faslodex for the same reasons. The high positivity of hormone receptors is one of the essential criteria for the choice of hormone therapy, as well as the low level of Ki67, according to our results. We have also found that there is a good reason to supplement with calcium, and vitamin D3, as well as the prescription of bisphosphonates as a preventive measure for patients on aromatase inhibitor (AI). Most people ask for a BMD before starting treatment for an AI.

5. CONCLUSION

This study reveals an objective response rate of 38% at 6 months on hormone therapy, with an overall clinical benefit of 80%. The results indicate that, although the observed response rate is lower than that of the treatments documented in some previous studies, hormone therapy remains an effective option for the control of RH+/HER2-metastatic disease. The tolerance to the treatment is generally good, with mainly moderate adverse reactions, such as hot flashes. The patients also report an improvement in their general condition and a preserved quality of life despite the side effects. These observations support the continued use of hormone therapy as a first-line treatment for this type of cancer, while emphasizing the need for careful management of adverse reactions and continuous communication with patients about expectations and possible treatment adjustments.

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

To cite the article: Boudersa A et al. Evaluation of First-Line Endocrine Therapy for HR+/HER2- Metastatic Breast Cancer: Efficacy, Tolerance and Prescribing Practices. A Prospective and Observational study. Batna J Med Sci 2024; 11(4): 482-486

Abbreviations:

AI: Aromatase inhibitor
BMD: Bone Mineral Density test
CME: Continuing medical education
ER: Estrogen receptor
HER2-: Human epithelial growth factor receptor 2
HR+: Hormone receptor positive
HT: Hormone therapy
MBC: metastatic breast cancer
ORR: Objective response rate
PR: Progesterone receptor

REFERENCES

1. Delgado A, Guddati AK. Clinical endpoints in oncology - a primer. Am J Cancer Res. 2021 Apr 15;11(4):1121-1131
2. Robertson, John FR, et al. "A meta-analysis of clinical benefit rates for fulvestrant 500 mg vs. alternative endocrine therapies for hormone receptor-positive advanced breast cancer." Breast Cancer 26 (2019): 703-711.
3. phigénie Cavadias, Roman Rouzier, Florence Lerebours, Delphine Héquet, Bouffées de chaleur et cancer du sein avec récepteurs hormonaux positifs : mécanismes et prise en charge,Bulletin du Cancer,Volume 107, Issue 11,2020, Pages 1171-1185.
4. C Lhommé, P Pautier, L Zagamé, S Taïeb, P Descamps, S Delaloge, P Morice, P Petrow, P Duvillard, Surveillance de l'endomètre des femmes sous tamoxifène, Gynécologie Obstétrique & Fertilité,Volume 31, Issues 7–8,2003,Pages 647-656,ISSN 1297-9589,https://doi.org/10.1016/S1297-9589(03)00195
5. Thorne C. Management of arthralgias associated with aromatase inhibitor therapy. Curr Oncol. 2007 Dec; 14 Suppl 1(Suppl 1):S11-9. doi: 10.3747/co.2007.152. PMID: 18087604; PMCID: PMC2140182.
6. Recommandations françaises de stratégies thérapeutiques pour la prévention et le traitement de l'ostéoporose induite par les traitements adjuvants du cancer du sein, B.Bouvard et al./Revue du rhumatisme 86(2019) 426-437, Elsevier.
7. A.R. Ferreira, A. Di Meglio, B. Pistilli, A.S. Gbenou, M. El-Mouhebb, S. Dauchy, C. Charles, F. Joly, S. Everhard, M. Lambertini, C. Coutant, P. Cottu, F. Lerebours, T. Petit, F. Dalenc, P. Rouanet, A. Arnaud, A. Martin, J. Berille, P.A. Ganz, A.H. Partridge, S. Delaloge, S. Michiels, F. Andre, I. Vaz-Luis,
8. Differential impact of endocrine therapy and chemotherapy on quality of life of breast cancer survivors: a prospective patient-reported outcomes analysis,
9. Annals of Oncology, Volume 30, Issue 11, 2019, Pages 1784-1795,ISSN 0923-7534, https://doi.org/10.1093/annonc/mdz298

To cite the article: Boudersa A et al. Evaluation of First-Line Endocrine Therapy for HR+/HER2- Metastatic Breast Cancer: Efficacy, Tolerance and Prescribing Practices. A Prospective and Observational study. Batna J Med Sci 2024; 11(4): 482-486