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COMPLETE REMISSION OF AN ADVANCED HORMONE RECEPTOR POSITIVE HER2 NEGATIVE BREAST CANCER TREATED BY FIRST LINE PALBOCICLIB-LETROZOLE AND LOCAL TREATMENT
Zineb Benbrahim, Department of Medical Oncology, Hassan II University Hospital, Fez, Faculty of Medicine and Pharmacy of Fez, University Sidi Mohammed Ben Abdellah, Fez, Morocco. Lamiae Amaadour, Department of Medical Oncology, Hassan II University Hospital, Fez, Faculty of Medicine and Pharmacy of Fez, University Sidi Mohammed Ben Abdellah, Fez, Morocco. Karima Oualla, Department of Medical Oncology, Hassan II University Hospital, Fez, Faculty of Medicine and Pharmacy of Fez, University Sidi Mohammed Ben Abdellah, Fez, Morocco. Amina Alj, Nakhil Center of Nuclear Medicine, Rabat, Morocco. Samia Arifi, Department of Medical Oncology, Hassan II University Hospital, Fez, Faculty of Medicine and Pharmacy of Fez, University Sidi Mohammed Ben Abdellah, Fez, Morocco. Chahrazed Bouchikhi, Department of Gyneco-Obstetrics, Faculty of Medicine and Pharmacy of Fez, University Sidi Mohammed Ben Abdellah, Fez, Morocco. Nawfel Mellas, Department of Medical Oncology, Hassan II University Hospital, Fez, Faculty of Medicine and Pharmacy of Fez, University Sidi Mohammed Ben Abdellah, Fez, Morocco.

Corresponding author: Zineb Benbrahim, Department of Medical Oncology of Hassan II University Hospital.Route Sidi Hrazem, Fez, Morocco. Email: email,zineb.benbrahim@usmba.ac.ma

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Z. Benbrahim, L. Amaadour, K. Oualla, A. Alj, C. Bouchikhi and N. Mellas

ABSTRACT

The palbociclib-letrozole combination has revolutionized the treatment of Hormone-receptor-positive Her2-negative advanced breast cancers. The aim of the inclusion of targeted agents in endocrine based therapy is to prolong hormonsensitivity and to delay the initiation of subsequent chemotherapy, especially for patients with low disease burden. However, the interest of locoregional treatment after response to initial therapy in advanced disease still investigational especially in the era of biotherapy. In the present case report, we showed the possible complete response with hormone-therapy associated to targeted therapy and highlighted the role of loco-regional treatment in this situation.

INTRODUCTION

Breast cancer is the most common cancer among females in the worldwide [1, 2]. Hormone-receptor-positive Her2-negative breast cancers represent approximately 60% of breast cancers [3]. Data show that Palbociclib associated with hormone-therapy in postmenopausal females increased the response rate and progression free survival in the locally advanced or metastatic settings of these luminal tumours [4]. However, the impact of locoregional treatment in advanced stages, on survival is still debated, especially in when a complete response is achieved after initial medical treatment. This case showed a complete response with this treatment and highlights the role of loco-regional treatment in this situation.

CASE REPORT

A 52-year-old woman with no past medical history was admitted to our breast unit due to a slowly progressive small lump in her right breast. Physical Examination revealed a 3 cm nodule on the upper right quadrant. Breast ultrasonography and mammography described an irregular ACR 5 breast lesion with axillary and subclavicular ipsilateral lymphadenopathies. A core needle biopsy of breast lesion was performed. Histology showed invasive ductal carcinoma, grade II SBR, Eostrogen and progesteron receptors positive at 90% and 10% respectively, Her2neu negative. A staging workup by thoracic and abdominal scan (TA scan) was performed with imaging results of lymph node metastases to the right axilla. CA15-3 marker was negative. As a consequence of these results, a PET computed tomography scan was performed which showed active lesions in the right subclavicular region, mediastinum and the 7th thoracic vertebrae (figure 1). So, first line Letrozole palbociclib combination was started and it was well tolerated. After three months of therapy, physical examination revealed a decrease of breast lesion to 1cm vs 3cm. Pet scan showed complete regression of previous active lesions (figure 2). We continued three other months of the same therapy to maintain the benefit. Pet scan control after 6 months of treatment initiation revealed no signs of disease spread (figure 3). So, the patient underwent radical surgical treatment with mastectomy and axillary node dissection followed by whole breast radiotherapy and stereotaxic radiotherapy on the 7^{th} vertebrae. Histological examination described a residual tumoral disease of 1.5cm with negative surgical margins and 5 involved adenopathies among 13 excised. After international multidisciplinary discussion, we decided to restart letrozole palbociclib combination on the adjuvant setting. The patient is still on stable complete response after one year of treatment.

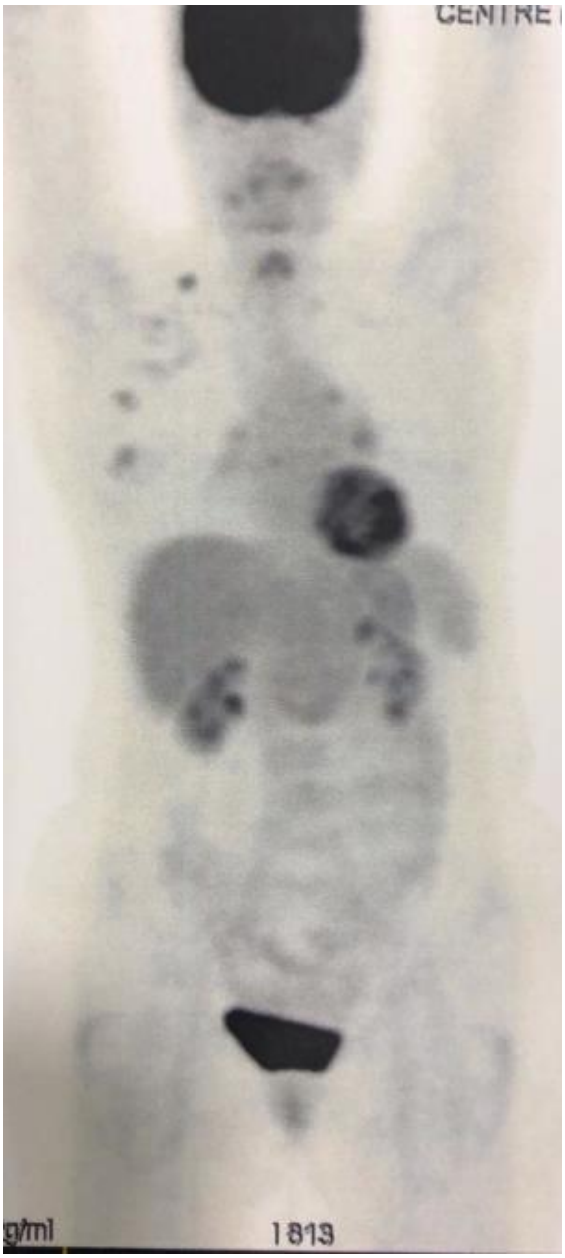

Figure 1 : Pet CT before treatment initiation : lymph nodes and vertebral metastases

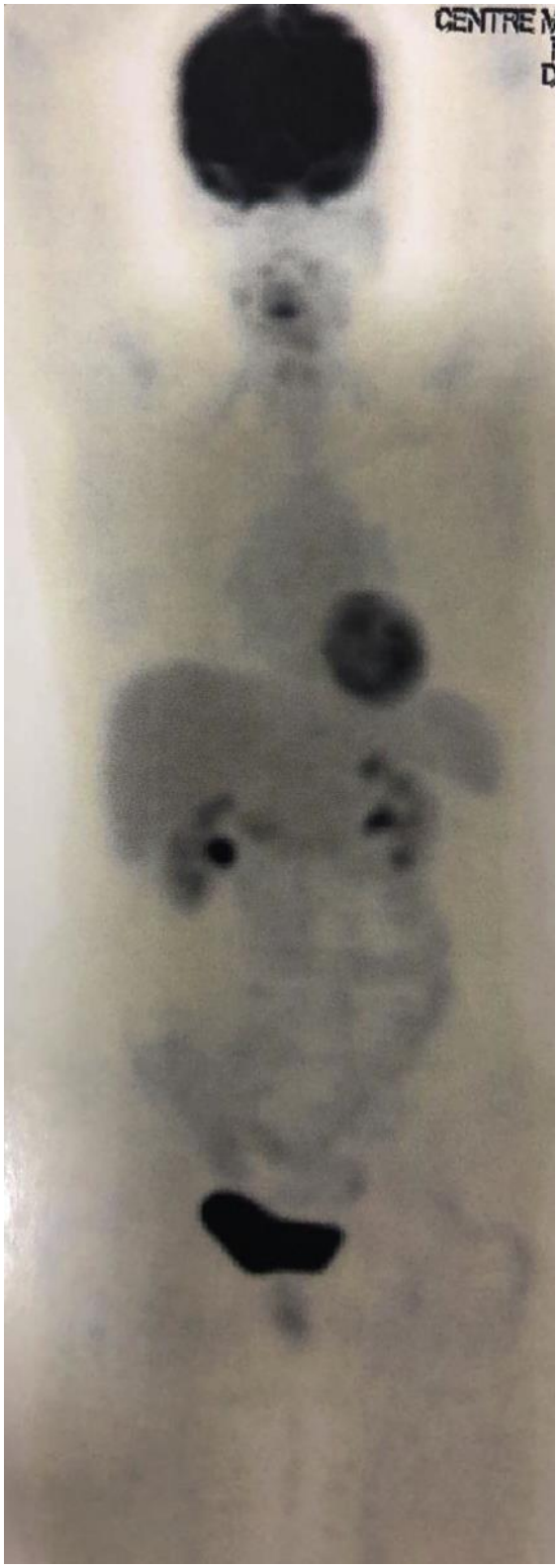

Figure 2 : Pet scan imaging 3 months after treatment initiation : metabolic complete response

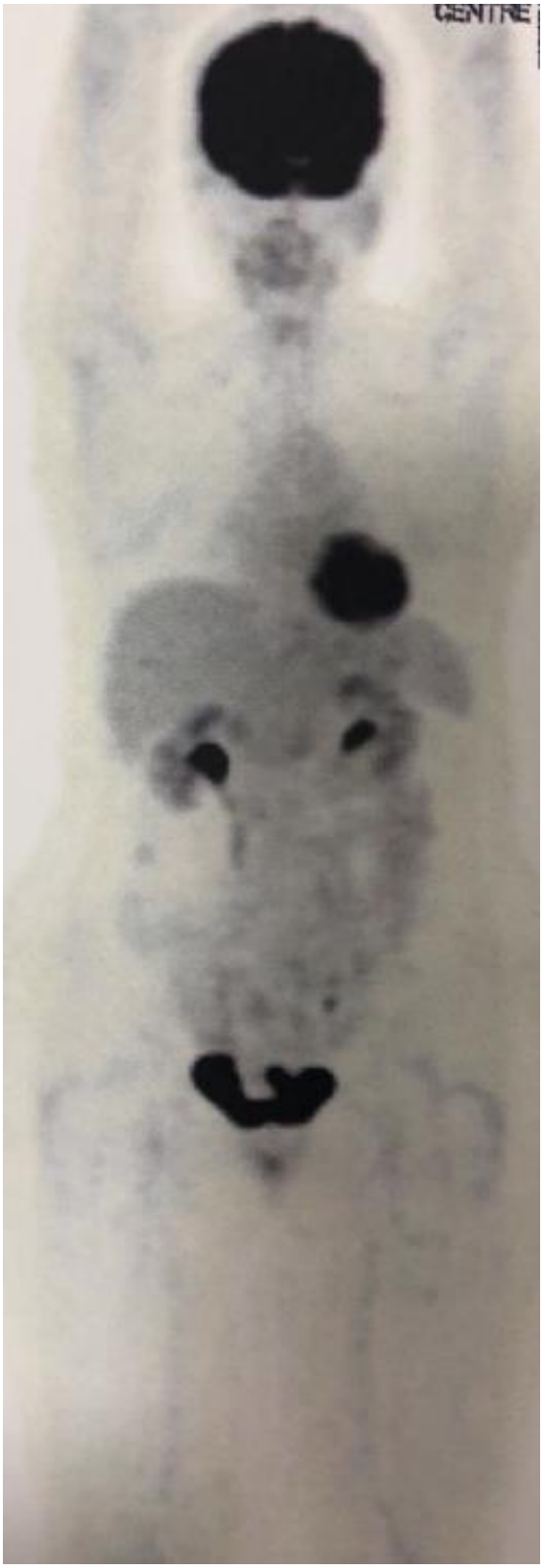

Figure 3 : Pet scan imaging 6 months after treatment initiation : maintained metabolic complete response

DISCUSSION

Palbociclib is a second-generation inhibitor of cyclin-dependent kinases (CDK) 4 and 6. It regulates the cell cycle through phosphorylation of the retinoblastoma protein (Rb) and inactivation of Rb function as a tumor suppressor [5].

The development of palbociclib for the treatment of luminal breast cancer was based on the identified dependence of luminal breast cancer on CDK4/6 signaling and a synergistic effect from targeting the ER, cyclin-D–CDK4/6–Rb pathway [6].

Palbociclib is approved by the Food and Drug Administration (FDA) in combination with endocrine therapy for the treatment of postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer [7]. This approval is based on the results of PALOMA-2 study that concluded to an increase in progression-free survival in first line treatment with Palbociclib plus Letrozole versus letrozole alone [8]. In this trial, the objective response rate in the Palbociclib based combination was approximately 42%, however the complete response rate is unknown [8]. In the present case report the metabolic complete response rate was obtained after only 3 months of Palbociclib-Letrozole treatment. Durable response justified a locoregional treatment of the breast. Data evaluating the benefit of such a strategy have yielded controversial results. An Indian trial concluded to no difference in overall survival between surgery and standard postoperative radiation versus no locoregional treatment in 350 women who achieved partial or complete response to anthracyclines [9]. By contrast, in a Turkish trial, 274 women with metastatic breast cancer were randomly assigned to local management followed by systemic therapy versus systemic therapy only [10]. Patients treated with local management experienced an improvement in five-year survival with locoregional treatment. Of note, patients in the surgical group had lower rates of triple-negative disease (7 versus 17 percent) and had more frequently bone metastases only (33 versus 20 percent). The subgroup analysis showed that patients with hormone-positive, HER2-negative disease; younger than 55 years; and those without visceral metastases appeared to derive the greatest benefit from local management [10]. For the latter reasons, we thought our patient would be a good candidate for surgery and adjuvant radiotherapy (52years old, no visceral metastases and high expression of hormone receptors).

Although our patient had metabolic complete response, she did not achieve an histological complete response. This raised the concern of adjuvant systemic treatment and whether to continue the same regimen or to offer chemotherapy. Data supporting such an approach are lacking. We continued palbociclib with letrozole on the basis of the patient preference and to privilege her quality of life.

CONCLUSION

In the present paper we showed that Palbociclib associated with hormonetherapy may lead to high response rates and durable long disease-free period. This can allow a local treatment that helps to maintain such a complete response. However, studies are needed to define the most appropriate patients for multimodal treatment.

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