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# Exceptional Metabolic Response to Ribociclib and Letrozole in a Young Patient With De Novo Multimetastatic Luminal A Pleomorphic Lobular Breast Cancer: A Case Report

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## Abstract

Metastatic breast cancer (MBC) with a luminal A profile typically follows an indolent clinical course. However, the pleomorphic lobular subtype can manifest aggressive biology with an atypical dissemination pattern and high tumor burden. We report a case of a 42-year-old female diagnosed with de novo luminal A MBC, characterized by an exuberant multimetastatic state involving multiple visceral organs, serosal surfaces, soft tissues, and the axial and appendicular skeleton. Given this high tumor burden, the patient initiated first-line therapy with the CDK4/6 inhibitor ribociclib in combination with letrozole and goserelin. A near-complete metabolic response was observed across all sites monitored by PET/CT after seven months of treatment. This case highlights the clinical efficacy of combining CDK4/6 inhibitors with endocrine therapy even in scenarios of aggressive, high-volume multimetastatic disease.

**Categories:** Oncology

**Keywords:** cdk4/6 inhibitors, fdg pet/ct, luminal a breast cancer, metastatic breast cancer, pleomorphic lobular carcinoma, ribociclib

## Introduction

Invasive lobular carcinoma (ILC) accounts for approximately 10-15% of all breast cancers [1]. It is characterized by a loss of E-cadherin expression, leading to a lack of cellular adhesion and a unique propensity for metastasis to atypical sites, such as the gastrointestinal tract, peritoneum, and pancreas [2,3]. The pleomorphic variant of ILC (PLC) is a distinct, aggressive subtype associated with higher histological grades and a worse prognosis compared to classic ILC [4,5].

While CDK4/6 inhibitors (CDK4/6i) combined with endocrine therapy (ET) are the established standard of care for hormone receptor-positive (HR+), HER2-negative metastatic breast cancer (MBC), most notably luminal A disease, a molecular subtype typically characterized by high hormone receptor expression and lower proliferative activity, managing patients with a massive de novo tumor burden remains a clinical challenge [6,7]. This challenge arises because endocrine-based targeted regimens traditionally exhibit a slower onset of response compared to cytotoxic chemotherapy, raising concerns when rapid debulking or disease control is required. This is particularly critical in young patients, in whom the disease often presents with more aggressive features [8]. We report a profound clinical and radiological recovery in a young patient with luminal A PLC presenting with a massive initial tumor burden.

## Case Presentation

In June 2025, a 42-year-old female presented to the medical oncology department with an exophytic, ulcerated, and exuberant lesion on the left breast, which she reported having noticed approximately six months prior to presentation. Over the preceding two months, she developed severe, debilitating, generalized back pain that progressively restricted her mobility, resulting in an initial Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 3 [9]. On physical examination, the left breast demonstrated a large ulcerated exophytic tumor with associated ipsilateral axillary lymphadenopathy. Abdominal examination revealed a soft, non-tender abdomen without clinically palpable hepatosplenomegaly or ascites.

Baseline laboratory evaluation revealed mild normocytic anemia, elevated total serum calcium (11.2 mg/dL) and serum alkaline phosphatase (280 U/L), along with mildly elevated liver transaminases (aspartate aminotransferase {AST}: 58 U/L, alanine aminotransferase {ALT}: 62 U/L) and total bilirubin within normal limits. Baseline tumor markers were marked by an elevated CA 15-3 level (245 U/mL).

The breast biopsy revealed invasive carcinoma G3, ER: 100%, PR: 100%, HER2-negative (0), and Ki-67: 10%.

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A subsequent biopsy of a bone lesion confirmed metastasis by breast carcinoma with pleomorphic lobular characteristics (E-cadherin negative/aberrant) and a Ki-67 of 30%, highlighting clonal evolution [10]. The 18F-fluorodeoxyglucose (18F-FDG) PET/CT in May 2025 demonstrated extensive multimetastatic disease, involving the pancreas, liver, peritoneum, and axial and appendicular skeleton (Figure 1). The brain MRI at diagnosis showed multiple lytic lesions in the calvaria without intracranial invasion (Figure 2).

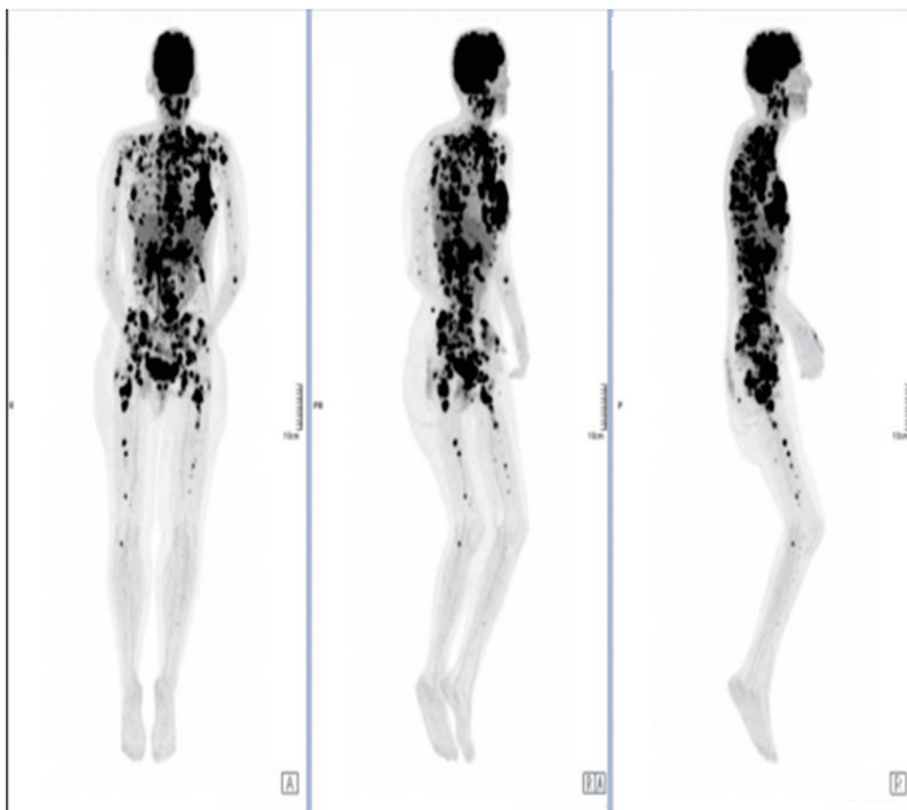


**FIGURE 1: Baseline 18F-FDG PET/CT (May 2025).**

Exuberant metabolic activity is observed in the left breast, pancreas, peritoneum, and axial skeleton, characterizing a high-volume multimetastatic disease.

FDG: fluorodeoxyglucose

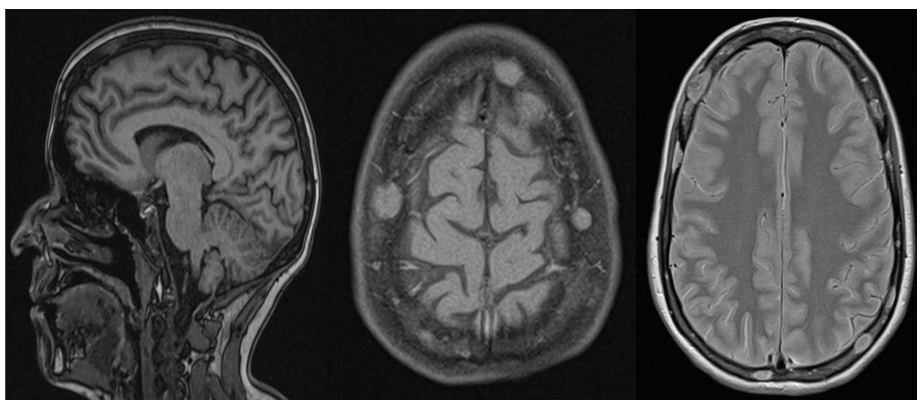


**FIGURE 2: Brain magnetic resonance imaging (MRI) at diagnosis.**

Sagittal T1-weighted image showing a lytic lesion in the posterior parietal region without dural involvement (left). Axial T1-weighted sequence with fat suppression showing multiple hyperintense metastatic foci in the calvaria (center). Axial T2-weighted/PD image confirming bone involvement without scalp or intracranial invasion (right).

PD: proton density

The patient initiated goserelin, ribociclib (600 mg daily on a three-weeks-on/one-week-off schedule), and letrozole (2.5 mg daily) in June 2025. The clinical response was rapid, with significant pain relief and functional improvement. By February 2026, the patient reached an ECOG PS of 0. A follow-up PET/CT in January 2026, seven months after treatment initiation, confirmed near-complete metabolic resolution of all visceral, peritoneal, and bone lesions, along with normalized tumor markers (CA 15-3: <25 U/mL) and liver/bone laboratory parameters (Figure 3). This objective response was characterized by a significant overall attenuation of metabolic activity, with a drastic reduction from the initial high baseline uptake (baseline maximum standardized uptake value {SUVmax} of 29.5). Malignant metabolic activity persisted mainly in the primary left breast lesion, with some residual but equivocal viability noted in bilateral axillary nodes, left femur, and pelvic bones, while the remainder of the examination showed no metabolic evidence of malignancy.

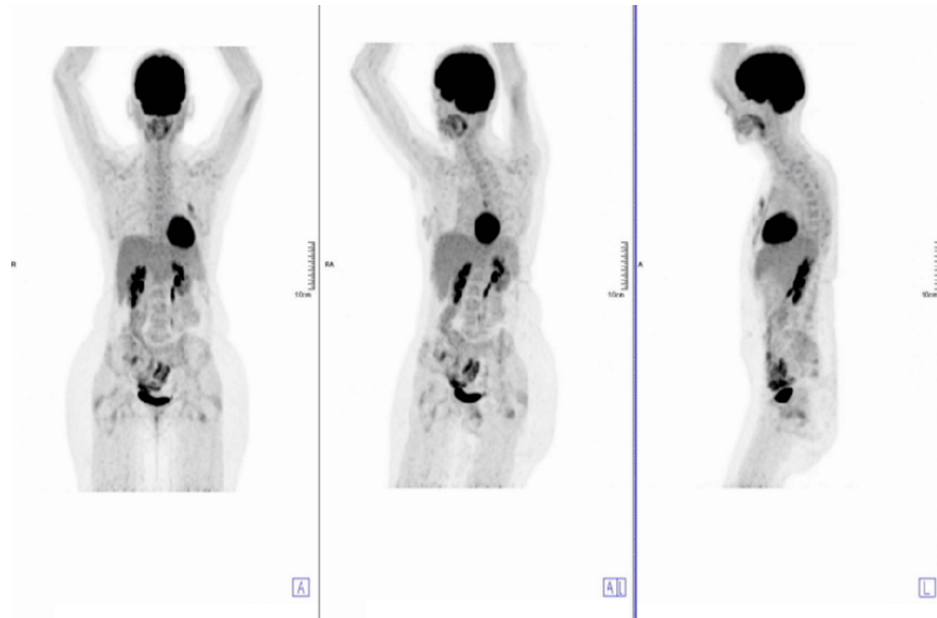


**FIGURE 3: Follow-up 18F-FDG PET/CT (January 2026).**

Near-complete metabolic resolution of the multiorgan tumor burden after seven months of treatment with ribociclib and letrozole.

FDG: fluorodeoxyglucose

## Discussion

Pleomorphic variant of invasive lobular carcinoma (PLC) is a molecularly distinct entity that combines the discohesive growth of invasive lobular carcinoma (ILC) with the aggressive nuclear features and high proliferation of high-grade ductal carcinomas [4,11]. The discordance in Ki-67 between the primary tumor and metastatic sites observed in our patient is a known phenomenon in PLC, reflecting its potential for rapid progression [12]. Despite maintaining a strong hormone receptor-positive profile (ER: 100%, PR: 100%) indicative of a luminal A-like surrogate, the disease behaved clinically like a highly aggressive phenotype, resulting in severe multimetastatic de novo dissemination involving visceral organs, soft tissues, and the skeleton.

The presentation of such a massive initial tumor burden often poses a significant therapeutic dilemma. Historically, clinicians might have favored upfront cytotoxic chemotherapy for patients with extensive symptomatic multimetastatic disease. However, current evidence suggests that unless a "visceral crisis" (imminent organ failure) is present, ET plus a CDK4/6i should be the first-line preference [13].

Our patient's exceptional outcome strongly supports this approach. The decision to initiate ribociclib combined with letrozole and ovarian function suppression (goserelin) avoided the significant toxicities associated with systemic chemotherapy while achieving a remarkable clinical response. Importantly, the regimen was exceptionally well tolerated; throughout the seven months of treatment at the full 600 mg dose, the patient experienced no grade 3 or 4 adverse events, maintained normal QTc intervals on serial electrocardiograms, exhibited stable blood counts without severe neutropenia, and did not require any dose reductions or treatment interruptions. The MONALEESA-7 trial, focusing on premenopausal women, showed that ribociclib plus ET significantly improves overall survival (OS) and progression-free survival (PFS) [14,15]. Furthermore, data from the MONALEESA-2 and MONALEESA-3 trials support the use of

ribociclib across various subgroups, including those with visceral involvement and de novo presentation [16,17].

The rapid metabolic response (seven months) in our patient, documented by 18F-FDG PET/CT, aligns with emerging evidence that early metabolic changes can predict long-term progression-free survival in patients on CDK4/6i [18,19]. Finally, the RIGHT trial has recently reinforced this strategy, demonstrating that ribociclib plus endocrine therapy is superior to physician's choice chemotherapy in achieving progression-free survival in patients with HR+/HER2-negative metastatic breast cancer and aggressive disease features [20].

## Conclusions

The combination of CDK4/6 inhibitors with endocrine therapy can induce profound clinical and metabolic responses in patients with de novo multimetastatic breast cancer. While longer follow-up is necessary to establish the long-term durability of these outcomes, precise histological diagnosis remains essential to personalize treatment strategies. This case highlights the efficacy of ribociclib in achieving near-complete metabolic remission in a young patient with high-volume disease, corroborating recent clinical trial data that favor targeted therapy over chemotherapy even in aggressive scenarios.

## Additional Information

### Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

**Concept and design:** Inês Ângelo, Isabel Fernandes, Daniela Costa, Alexandra Roque, Idília Pina, Carolina Trabulo, Carolina Xavier, Angelica Micolo, Sara Morais

**Acquisition, analysis, or interpretation of data:** Inês Ângelo, Isabel Fernandes, Daniela Costa, Alexandra Roque, Idília Pina, Carolina Trabulo, Angelica Micolo, Sara Morais

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**Critical review of the manuscript for important intellectual content:** Inês Ângelo, Isabel Fernandes, Daniela Costa, Alexandra Roque, Idília Pina, Carolina Trabulo, Carolina Xavier, Angelica Micolo, Sara Morais

**Supervision:** Inês Ângelo, Isabel Fernandes, Idília Pina

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