

# Case report: A durable response to Anastrozole re-challenge with Everolimus in a patient with advanced-stage estrogen receptor-positive breast cancer

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### ABSTRACT

Estrogen receptor-positive breast cancer is a heterogeneous disease characterized by its dependence on estrogen for growth and progression. Although hormonal therapy remains the cornerstone of treatment, many patients eventually develop resistance, leading to recurrence and disease progression. This case report describes a durable response to a rechallenge with Anastrozole (Arimidex) in combination with Everolimus (Afinitor), an mTOR inhibitor, in a patient with advanced (stage IV) ER+ metastatic breast cancer.

**Keywords:** stage IV ER+ breast cancer, mTOR inhibitor, treatment rechallenge

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## INTRODUCTION

Estrogen receptor-positive breast cancer is a heterogeneous disease characterized by its dependence on estrogen for growth and progression. Although hormone therapy remains the mainstay of treatment, many patients eventually develop resistance, leading to disease recurrence and progression.

## CASE PRESENTATION

The patient, diagnosed with IV ER+, PR-, HER2- breast cancer in February 2010, was a schoolteacher at the time of her initial diagnosis and is now retired. She has no history of smoking, active alcoholism, or drug abuse. Throughout her life, she has maintained a healthy lifestyle with regular physical activity and a varied diet.

However, she neglected her diet and exercise for 1.5 years following the death of her oldest son in mid-2004.

Imaging studies at presentation revealed an 11-cm primary tumor in the left breast, axillary involvement, and three metastases to vertebrae T4 and T5, measuring between 6 mm and 18 mm. She received first-line treatment with Anastrozole (Arimidex) as an aromatase inhibitor and Clodronate (Bonefos) as bone-targeted therapy.

The patient achieved a durable response to Anastrozole, resulting in a stable disease lasting over eight years. However, the disease progressed with the emergence of five new liver metastases, ranging from 3 mm to 17

mm. Second-line hormonal therapy with Exemestane resulted in further three-year disease control.

As the disease progressed further, the number of liver and bone metastases increased, with new metastases to the skull and femur identified, measuring between 8 mm and 16 mm. Metastases in all liver segments were observed, ranging from 7 mm to 23 mm. Liver function tests showed significantly elevated values (Gamma-GT: 344 UI/L; ALAT: 602 U/L; ASAT: 542 U/L). A third-line hormonal therapy with Megestrol Acetate (Megace) was administered without response. Despite continued progression, the primary tumor and metastatic lesions remained strongly ER+ (67-84%), as evidenced by a new biopsy.

Resistance mechanisms are plausible given the patient's prior response to Anastrozole. The treating physician decided to rechallenge the patient with Anastrozole, adding Everolimus (Afinitor) to block downstream signaling pathways, thereby increasing the likelihood of a positive response to hormonal therapy.

Follow-up imaging after six weeks of treatment showed no evidence of disease progression in the primary tumor, bony metastases, or liver metastases, indicating stable disease.

Liver function values returned to acceptable ranges, with Gamma-GT at 48 UI/L, ALAT at 51 U/L, and ASAT at 49 U/L at the last measurement in May 2024.

The patient remains stable (NEAD) three years down the line, as of June 2024, and returns for quarterly scans.

## DISCUSSION

This case illustrates the potential for a durable response by rechallenging hormonal therapy in ER+ advanced-stage breast cancer. One of the most pressing challenges in managing this disease is resistance to hormone therapy; however, combining hormonal therapy with targeted agents may overcome key biological mechanisms of resistance and improve patient outcomes.<sup>1,2</sup>

The combined Everolimus (Afinitor) and Anastrozole (Arimidex) may have enhanced the anti-tumor response of hormonal therapy by inhibiting signal transduction pathways critical for tumor growth and survival.<sup>3</sup> Although this case is promising, as it aligns with

previous research<sup>4</sup>, further studies are needed to determine the optimal combinations and sequences of therapies that will benefit patients with advanced-stage ER+ breast cancer.<sup>5,6</sup>

## CONCLUSIONS

The case highlights the effectiveness of rechallenging hormonal therapy combined with targeted agents in patients with advanced-stage ER+ breast cancer who develop resistance to previously administered treatments. The findings underscore the need for further research to identify and verify optimal combinations and sequencing to achieve maximum efficacy in these patients.

**Ethical Clearance:** Since this was a case study where no personal data that could identify the patient were transmitted to the author, and since the patient was not subjected to any assessments beyond the standard of care, this case study did not require ethical approval other than the consent of the treating GP to use the pseudonymized data.

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