Eribulin combined with radiation therapy in a young patient re-irradiated for a new lesion of breast cancer

Oulimata Dieng¹, Valerie Laurence², Christelle Logerot¹, Youlia Kirova¹,³

¹Departement of Radiation Oncology, ²Department of Medical Oncology, Institut Curie, Paris, ³University Versailles St Quentin, France

Corresponding author:

Youlia M. Kirova, M.D.,
Department of Radiation Oncology,
Institut Curie,
26 Rue d’Ulm,
75005 Paris, France
Tel : 33144324000
Email: youlia.kirova@curie.fr

No Grants support

No conflict of interest.

Key words: breast cancer, concurrent eribulin radiotherapy, adverse effects.
ABSTRACT

Eribulin is widely used in the treatment of metastatic breast cancer, with a manageable toxicity profile. This aggressive disease often requires systemic and local treatments, comprising surgery or radiotherapy. However, eribulin is usually discontinued during radiation therapy due to the lack of data concerning the safety of this combination, especially in the setting of repeat locoregional radiation therapy.

Our patient was diagnosed with ER-positive invasive ductal carcinoma of the left breast initially treated by surgery, radiation therapy, chemotherapy and hormone therapy. She then received various lines of chemotherapy for multiple triple-negative relapses in the left axillary region. Since October 2020, she has been treated by eribulin. In order to improve local control, it was decided to add local radiation therapy to the region of recurrence in addition to systemic therapy. She underwent radiation therapy concomitantly with eribulin from February to March 2021. Treatment was very well tolerated and no acute toxicity was reported. This is the first published case of repeat local radiation therapy in combination with eribulin.
INTRODUCTION

Eribulin is a non-taxane agent that inhibits microtubule polymerization without blocking depolymerization, causing tubular sequestration into non-productive aggregates. It is a structurally modified synthetic analogue of Halichondrin B, a natural product isolated from the marine sponge *Halichondria okadai* (1).

The phase III EMBRACE study (2) showed significant improvement in overall survival with eribulin compared to treatment of physician’s choice in heavily pretreated patients with metastatic breast cancer, which was the basis for approval of eribulin for the treatment of metastatic breast cancer patients who had progressed after at least two prior chemotherapy regimens, including an anthracycline and a taxane.

The benefits of eribulin are achieved with a manageable toxicity profile, as the most common adverse events are fatigue and neutropenia.

However, few data are available concerning the safety of eribulin administered concomitantly with radiation therapy. In this article, we report, for the first time, the case of a patient with metastatic breast cancer treated with eribulin in combination with local radiation therapy for oligoprogression of a tumor in the left axillary region, previously irradiated at full therapeutic dose.

**Patient’s history**

In 2006, this 26-year-old woman was first diagnosed with a hormonal receptor (HR)-positive invasive ductal carcinoma of her left breast. She had no previous medical history. Her
mother had died at the age of 60 from malignant glioblastoma. Due to her age at the time of diagnosis, she was tested for BRCA1 and BRCA2, but no gene mutations were detected. She underwent total mastectomy together with axillary lymph node dissection with 8 positive lymph nodes out of 11 nodes removed, with invaded surgical margins. She then received adjuvant chemotherapy (3 FEC-100 regimen and docetaxel), followed by tamoxifen initiated in August and continued for 5 years. She received radiation therapy with a dose of 50 Gy in 25 fractions to the left chest wall and regional lymph nodes (levels 1-4, internal mammary chain and interpectoral nodes) using the previously described technique (3), with no toxicity. Five years later, she was diagnosed with left axillary lymph node relapse and lung metastases. Axillary lymph node biopsy revealed metastasis of a HR--positive carcinoma. Chemotherapy with paclitaxel+bevacizumab+leuprorelin every 3 weeks was initiated. In December 2012, after 9 cycles, a partial response was obtained, and paclitaxel was discontinued and replaced by exemestane. In August 2013, bevacizumab was suspended due to proteinuria. She was then treated with (palbociclib+fulvestrant+leuprorelin). Twelve years after the initial diagnosis, a new triple-negative (TN) lesion in the same left axillary region was detected and a new regimen was initiated. Treatment was switched to capecitabine 1500 mg twice daily and left axillary adenectomy was performed in October 2019. Repeat radiation therapy to the axillary region was considered at that time, but was finally not performed. In April 2020, another relapse was detected in the left axillary region (confirmed by biopsy) and a new line of therapy with paclitaxel and atezolizumab (Temporary Authorization for Use) was initiated.
Evaluation after 6 cycles showed progression of one left axillary node.

In October 2020, the chemotherapy regimen was therefore switched to eribulin 1.4 mg/m² on day 1 and day 8 every 3 weeks, which was very well tolerated.

She underwent another adenectomy in January 2021. The surgeon put clips in the tumor bed to guide the radiation therapy.

After further multidisciplinary discussion, due to multiple relapses in the same region despite numerous adenectomies and various lines of chemotherapy, and in view of the need to maintain systemic therapy, it was decided to deliver repeat radiation therapy to the left axillary region in order to improve local control while continuing eribulin. IMRT (25 fractions of 1.8 Gy to a total dose of 45 Gy) was administered to the tumor bed from 16 February to 22 March, concomitantly with eribulin (Figure 1). Treatment was delivered in the same position as the first radiation therapy, taking into account the doses previously received and was targeted to the adenectomy region. The sixth and seventh cycles of eribulin were administered on 25 February and 18 March, respectively.

She was reviewed by a radiation therapist once a week, and no adverse events were observed during treatment. The patient completed her radiation therapy with grade I radiodermatitis. Her subsequent treatment and follow-up were ensured by the medical oncologist.

Three months after the end of radiotherapy, the patient continues her systemic therapy with good quality of life and a PS of 0.

**DISCUSSION**

Very few published data are available concerning the concomitant use of eribulin and repeat local radiation therapy. Although eribulin is widely prescribed to patients with metastatic
breast cancer, the safety of eribulin in combination with radiation therapy remains uncertain due to the lack of evidence on a potential radiosensitizing effect. A study published in 2016 (4) concluded on a manageable safety profile of eribulin when combined with palliative radiation therapy in patients with metastatic breast cancer. Another case report of brain metastases from breast cancer treated by whole-brain radiotherapy and eribulin (5) found no unexpected acute toxicity of these two treatments.

The present case confirms that the combination of local radiation therapy (after surgery) using an adapted technique with eribulin that ensures perfect control of metastatic disease is safe and very well tolerated and illustrates the value of multidisciplinary management in these complex patients.

It is noteworthy that our young patient developed a second, triple-negative breast cancer, 12 years after being treated for ER-positive invasive ductal carcinoma. It is even more interesting that metastatic disease was controlled by systemic therapy; however, she experienced repeated relapses in the same axillary region. Local control plays an important role in tumor control and survival.

The ESME series, published in 2019, demonstrated an improvement in overall survival with exclusive radiotherapy, exclusive surgery or a combination of these two modalities compared to no locoregional treatment in patients with de novo metastatic breast cancer (6).

**In conclusion**, this first case of repeat local radiation therapy in combination with eribulin demonstrates the feasibility of this combination. New molecules now allow a longer life expectancy and it is important to know how to combine new molecules with radiation therapy. Further studies are needed to provide long-term data on the efficacy and safety profile of this combination.
REFERENCES


Figure 1: Irradiated volume

A. Currently irradiated volume of new lesion region using IMRT to total dose of 45 Gy/25 fractions. The clips put by the surgeon to guide the radiation therapy in the tumor bed are visible.
B: Total dose of previous post operative irradiation and the new irradiation