Long-Lasting Exceptional Radiological Complete Response after Treatment with Eribulin in a Patient with Triple-Negative Breast Cancer with Liver Involvement

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Keywords

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Abstract

We report the case of a 50-year-old woman with a triple-negative Ki67 80% breast cancer with liver metastases, who obtained a radiological long-lasting complete response after treatment with eribulin. The patient initially experienced progressive disease after a standard anthracycline/taxane-based adjuvant chemotherapy, a first-line treatment for metastatic disease with paclitaxel-bevacizumab, and a second-line maintenance treatment with bevacizumab and capecitabine. Eribulin was administered according to a 1.23 mg/m² scheme on days 1 and 8 every 3 weeks, and the treatment was always well tolerated. After 45 cycles of therapy, we still detected radiological evidence of complete response on liver sites of disease. This case report underlines the great efficacy of eribulin as third-line treatment for metastatic disease in a very aggressive form of breast cancer.

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Introduction

Breast cancer is the most frequent tumor in women, and in Italy it is responsible for 29% of cancer-related deaths in people under 50 years of age. The risk of breast cancer is usually age related; Italian women under 49 years of age have a 2.4% risk of developing breast cancer, while the probability increases to 4.7% in women aged between 50 and 69 or between 70 and 84 years [1]. Beyond age, there are many other well-known risk factors for breast cancer such as reproductive, hormonal, dietary, and metabolic causes [2–5]. In the last decades, many histopathological features have been identified to distinguish different types of breast cancer. Particularly, the expression of hormonal receptors (estrogen receptor [ER] and progesterone receptor [PgR]), the HER2 status, and the speed of cell proliferation, measured by Ki67 index, have emerged as important factors in breast cancer evaluation [6–10].

On the basis of these factors, breast cancer can be classified as Luminal-A, Luminal-B HER2 negative/positive, or triple-negative breast cancer (TNBC). Each class usu-

Fig. 1. Appearance of liver metastasis.

Fig. 2. Liver metastasis after 3 months of chemotherapy with eribulin.

Fig. 3. Complete disappearance of liver metastasis.

ally presents a specific diagnostic path, requires different treatments, and especially has a variable prognosis [11]. The most aggressive form is TNBC, which represents nearly 15% of all breast tumors, and is associated with a very poor prognosis [12–14].

Eribulin mesylate is a non-taxane microtubule inhibitor indicated for patients with locally advanced or metastatic breast cancer with evidence of progression after at least one prior chemotherapy regimen (2 prior chemotherapy regimens in Italy due to regulatory limitations) including an anthracycline and a taxane in an adjuvant or metastatic setting [15, 16]. In this report, we present the case of a 45-year-old woman with a triple-negative Ki67 80% breast cancer and liver metastases, who obtained a radiological long-lasting complete response after treatment with eribulin.

Case Presentation

In January 2011, a 45-year-old female was diagnosed with breast cancer and underwent a quadrantectomy with sentinel lymph node biopsy for a ductal invasive carcinoma. The tumor was characterized as highly undifferentiated, pT2N0, ER, PgR, and HER2 negative and with Ki67 70%. Due to the extreme aggressiveness of the tumor, the patient received an adjuvant chemotherapy with epirubicin (90 mg/m²) and cyclophosphamide (600 mg/m²) for 4 cycles every 21 days from April to June 2011, followed by docetaxel (100 mg/m²) for 4 cycles every 21 days from June to August 2011. The patient also underwent radiotherapy as adjuvant treatment on the remaining breast, and was subsequently followed with periodic visits.

In May 2013, the patient performed an abdominal ultrasound that highlighted 3 suspicious lesions in the liver. The presence of liver lesions (located in S-2, S-4 and S-8 measuring 14 × 14, 14 × 9, and 10 × 9 mm, respectively) was further confirmed by nuclear magnetic resonance imaging and by positron emission tomography-computed tomography (PET-CT). The histological examination after liver biopsy confirmed that the lesions were compatible with metastases of ductal invasive carcinoma ER negative, PgR negative, HER2 negative, Ki67 80%.

The patient received a first-line chemotherapy with paclitaxel (90 mg/m²; days 1, 8, and 15 of a 28-day-cycle) and bevacizumab (10 mg/m²; days 1 and 15 of a 28-day-cycle) that was started on 7 July 2013. After 3 months of therapy, the radiological restaging showed a significant dimensional reduction of all the 3 lesions (maximum diameter of 7 vs. 14 mm, 7 vs. 14 mm, and 5 vs. 10 mm, respectively, in S-2, S-4, and S-8, before and after treatment), and after 3 more months, a further partial response was observed (4–5 vs. 7 mm in S2, no change in S8, and S4 lesion no longer clearly identifiable).

The patient then started maintenance therapy with bevacizumab. After 3 months, a CT scan showed no change in hepatic lesions, but after 3 more months, 2 new hepatic metastatic nodules were detected in S-2 and S-8 (7 and 8 mm, respectively) (Fig. 1). A second-line chemotherapy with capecitabine (1,250 mg/m² bid, on days 1–14 of a 21-day-cycle) was started but was interrupted after 2 cycles for continuous diarrhea and hand-foot syndrome.

In November 2014, the patient started eribulin mesylate at the standard schedule of 1.23 mg/m² on days 1 and 8 every 3 weeks. We decided not to administer granulocyte colony-stimulating factors on day 9 given the good clinical condition of the patient (European Cooperative Oncology Group performance status [ECOG-PS]: 0). The first restaging after 3 months of therapy showed a significant regression of all the hepatic lesions, and some of them were no longer clearly visible (Fig. 2). After 3 additional cycles of chemotherapy, we observed a further dimensional reduction of the lesions (Fig. 3), and the restaging performed in September 2015 (after a total of 10 months of eribulin therapy)

showed a complete radiological response of all the hepatic nodules, subsequently confirmed by a PET-CT. Since then, the complete radiological response has continued, the patient has completed 45 cycles of treatment, and eribulin therapy is still ongoing at the same dose with no side effects and no occurrence of treatment delay due to adverse events. Considering the good tolerability profile of eribulin and the good current condition of the patient, we plan to continue the treatment until disease progression or unacceptable toxicity.

Discussion

Triple-negative breast cancer is a very heterogeneous disease, both on molecular and clinical level, characterized by a specific epidemiology and a distinct treatment path. TNBCs are frequently of high histological grade, are usually more prevalent among younger women and are much more aggressive and difficult to treat than hormone receptor-positive tumors, thus resulting in a higher risk of early relapse with visceral metastasis. In the metastatic setting, the usual first-line treatment is represented by taxane-based chemotherapy in association with bevacizumab; however, after the first line there is not a consensus strategy therapy: anthracycline-, platinum-, or capecitabine-based therapies are all possible options depending on the clinical condition of the patient.

The EMBRACE trial [15] is a phase 3, global, multicenter, randomized, open-label study that compared eribulin versus treatment of physician's choice (TPC) in 762 heavily pretreated women with locally advanced or metastatic breast cancer recruited from 135 centers between November 2006 and November 2008. The results of this trial showed that patients treated with eribulin had a significant improvement in overall survival (median OS 13.1 vs. 10.6 months; hazard ratio [HR] 0.81; $p = 0.041$), in progression-free survival (median PFS 3.7 vs. 2.2 months; HR 0.87; $p = 0.137$), as well as in overall response rate (ORR 12 vs. 5% $p = 0.002$) compared to those in the TPC arm. Eribulin treatment also showed a good tolerability profile: the most common adverse events in both arms were asthenia and fatigue (54 vs. 40%, respectively, for eribulin and TPC) and neutropenia (all-grade neutropenia 52% with eribulin vs. 30% with TPC). Treatment discontinuation was reported by 5% of all patients in the eribulin group due to the development of neuropathy. It is important to note that the median duration of eribulin treatment in the EMBRACE trial was 3.9 months (range 0.7–16.3) and that 59% of the patients received 5 or more eribulin cycles with a maximum of 23 cycles (range 1–23). In addition, in EMBRACE only 3 patients treated with

eribulin (from a total of 468, i.e. 1%) reported a complete radiological response.

Other recent publications have shown how radiological complete response is very difficult to achieve in heavily pretreated breast cancer patients. Lorusso et al. [17] conducted a “real world” study, analyzing taxane-refractory patients registered in the ESEMPIO database, which included 497 metastatic breast cancer patients treated with eribulin in Italy. Among 91 taxane-refractory patients, the analysis highlighted only one complete response using eribulin, with a median PFS of 3.1 months and median OS of 11.6 months.

Tanaka et al. [18] in a retrospective analysis of 29 patients treated with eribulin between 2011 and 2016, observed a median PFS of 90 days (95% confidence interval [CI] 67–126), a median OS of 264 days (95% CI 198–357), and only one case of complete response.

In our case report, at the time of writing this paper, the PFS of our patient is 34 months after 45 cycles of eribulin with absolute absence of side effects. To our knowledge, this is the longest treatment ever reported with eribulin and one of the few cases of pathological long-lasting exceptional complete response in a Ki67 80%, TNBC heavily pretreated patient. In our experience, eribulin can be considered an optimal therapeutic choice also in pretreated patients with highly aggressive breast cancer.

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Disclosure Statement

The authors declare that they have no conflicts of interest.

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