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Original article

Costs associated with Eribulin treatment for patients with metastatic breast cancer in a comprehensive cancer center in France

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ABSTRACT

Background: There is no standard recommendation for metastatic breast cancer treatment (MBC) after two chemotherapy regimens. Eribulin (Halaven®) has shown a significant improvement in overall survival (OS) in this setting. Its use may however be hampered by its cost, which is up to three times the cost of other standard drugs. We report the clinical outcomes and health care costs of a large series of consecutive MBC patients treated with Eribulin.

Methods: A monocentric retrospective study was conducted at Institut Curie over 1 year (August 2012 to August 2013). Data from patient's medical records were extracted to estimate treatment and outcome patterns, and direct medical costs until the end of treatment were measured. Factors affecting cost variability were identified by multiple linear regressions and factors linked to OS by a multivariate Cox model.

Results: We included 87 MBC patients. The median OS was 10.7 months (95%CI = 8.0–13.3). By multivariate Cox analysis, independent factors of poor prognosis were an Eastern Cooperative Oncology Group (ECOG) performance status of 3, a number of metastatic sites ≥ 4 and the need for hospitalization. Per-patient costs during whole treatment were €18,694 [CI 95%: 16,028–21,360], and €2581 [CI 95%: 2226–3038] per month. Eribulin administration contributed to 79% of per-patient costs.

Conclusions: Innovative and expensive drugs often appear to be the main cost drivers in cancer treatment, particularly for MBC. There is an urgent need to assess clinical practice benefits.

Introduction

Breast cancer (BC) is the most common cause of cancer deaths among women with 522,000 deaths worldwide in 2012, and remains one of the most costly cancers to treat [1,2]. Roughly 10–40% of new BC will develop metastatic breast cancer (MBC) whose prognosis remains poor with a median overall survival (OS) following the first metastatic event no longer than 2–3 years [3–5]. So far, there is no gold standard treatment defined for very advanced MBC [6,7].

Eribulin, an original inhibitor of microtubule dynamics, was approved in 2011 for the treatment of anthracycline and taxane refractory MBC. EMBRACE, Eribulin's phase III randomized pivotal study, demonstrated a statistically significant 2–3-months' improvement in OS as a primary endpoint when compared to treatment of physicians' choice [8]. Yet, these results were challenged by a different phase III randomized trial which failed to demonstrate Eribulin's superior efficacy when compared to capecitabine in a first to third line chemotherapy setting for MBC [9]. Ultimately, several European MBC clinical practice cohorts have shown consistent results on Eribulin efficacy as a third line chemotherapy with an acceptable tolerance profile [10–14], although real life survival in very advanced breast cancer patients

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remains low: about 4 months for progression-free survival, less than 6 months for post progression overall survival [15].

High costs are the main hindrance to using innovative drugs such as Eribulin. Eribulin is much more expensive than commonly administered cytotoxic drugs, many of which now have 'off-label' generic counterparts. For example, drug acquisition costs for both vinorelbine and gemcitabine are less than a third of Eribulin per-cycle costs: €375/$104, €541/$1086 and €1635/$4,513, respectively for vinorelbine, gemcitabine and Eribulin in France (in €2013) and in the USA (in $2011) [16]. The NICE (UK National Institute for Health and Care Excellence) judged that Eribulin was not cost-effective [16,17], concluding that Eribulin should not be recommended for use in MBC patients. Unsurprisingly, the cost-effectiveness study on Eribulin based on the EMBRACE trial (using a Markov model) reported that with a "willingness-to-pay" threshold of approximately $120,000 per QALY, Eribulin was not found to be affordable as compared to physician selected treatments [16]. More generally, it has been suggested that the use of recently approved chemotherapeutic agents has resulted in an incremental increase in drug price as well as toxicity, resulting in an increase in overall cost of treatment [18]. Within this context, our study aimed to assess clinical outcomes and healthcare costs of a large series of consecutive MBC patients treated with Eribulin in daily clinical practice in a comprehensive cancer center.

Methods

Study design

We conducted a retrospective study of MBC patients treated with Eribulin at Institut Curie, Paris, France. We enrolled women with MBC, who had consecutively received at least one infusion of Eribulin. Clinical outcomes and healthcare costs were collected during the treatment period which started on the date of the first Eribulin infusion and ended on the date of the decision to stop Eribulin, as noted in the medical record (regardless of cause). When the decision was not clearly recorded, the last infusion was registered instead. Overall survival was estimated as of June 2014 (datalock).

Data sources

We used the installed cytotoxic drugs prescription software (Chimio®, Computer Engineering, Paris, France) to identify all patients treated with Eribulin and to quantify infusion amounts. We used case records to collect medical information, patients' demographic data, and medical resources that were used. Two different authors checked for missing or inconsistent data and performed a second 10% random check across the whole database.

Medical data

We collected initial tumor characteristics including histological type, histological Elston and Ellis (EE) grading, hormonal (HR), and HER2 receptors status. Dates of first diagnosis and of first recorded metastatic event were retrieved. At the beginning of Eribulin therapy, we registered patients' Eastern Cooperative Oncology Group performance status (ECOG), body surface area (BSA), metastatic sites, and previous oncological treatments received for fighting metastatic disease. During the treatment period, we gathered the total dose of Eribulin administered, the number of administered cycles and infusions, and concomitant medications including granulocyte colony-stimulating factor (G-CSF) and bisphosphonates. A standard Eribulin protocol was used: infusion at day 1 and day 8 (in 21-day cycles) at a nominal dose of 1.4 mg/m^2. Clinically significant Eribulin-related adverse events were collected, including febrile neutropenia, anemia requiring blood transfusion, severe neuropathy (grade ≥ 2), and hospital admission for any cause. The causes of Eribulin treatment cessation were registered and qualified as disease progression (including death), Eribulin toxicity, or any other cause.

Identification and allocation of direct medical costs

Cost calculations were made, which quantified consumable resources for all patients in 2013 Euro (€). We estimated direct medical costs from the French health insurance perspective using diagnosis-related group fees (DRG). Assignment of patients to the DRG is based on the primary diagnosis (a classification system adapted from US billing codes). Day care hospitalization costs were directly matched to real DRG whenever possible; other stays were estimated with the official DRG fee structure. We entered fees for chemotherapy or radiation therapy sessions, blood tests, medical imaging, medical consultations, and for the unit price of Eribulin (2 ml vials containing 0.88 mg of the drug), as well as for the other drugs of interest (e.g. G-CSF, bisphosphonates) in the calculation model. The number of Eribulin vials used was derived from the total dose administered, body surface area (BSA) and number of infusions, as registered in the prescription software. Blood tests costs were calculated with a model based on local oncologists' knowledge of standard practices: liver function labs and blood electrolytes before every cycle, complete blood count before every infusion, and CA15.3 every three cycles.

Statistical analysis

Standard statistics were used to describe both continuous and discrete variables. Using the Kaplan–Meier method, OS was calculated as the time from the first Eribulin infusion to the date of death or last contact. A univariate Cox model identified factors linked to OS among variables relative to tumor and patient characteristics as well as adverse events. Variables at the level of significance of 10% were introduced in a multivariate Cox model and were retained in the final model at the level of significance of 5% after a top-down regression.

Cost measures were defined as median per-patient cost and median cost per patient per month during the treatment period. Factors of cost variability were identified by multiple linear regressions (ANCOVA) among the following variables: patient characteristics, presence of neutropenia or neuropathy, bone or brain metastasis (requiring radiation), number of metastatic sites, number and type of prior chemotherapy regimens for metastatic setting, number of Eribulin infusions, number of hospital days and BSA. Only significant variables at the level of 5% were retained in the final model.

A sensitivity analysis on costs tested three hypotheses: a 10% reduction of Eribulin unit fees, a scenario with only day care hospitalizations, and a scenario with maximum hospitalization stays (if Eribulin was widely used in most altered patients).

SAS® 9.3 Software (SAS Corp) was used for all statistical calculations.

Ethics

This study contained no modifications from standard practices in our institution. Our institutional review board and local ethics committee approved the study (authorization CNIL N°1737386). All patients provided written informed consent.