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Original article

Patient database analysis of fulvestrant 500 mg in the treatment of metastatic breast cancer: A European perspective

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ABSTRACT

Introduction: Clinical guidelines recommend that patients with hormone receptor (HR)-positive metastatic breast cancer (MBC) should be preferentially treated with endocrine therapy. Fulvestrant (a selective estrogen receptor degrader) is approved for use in these patients following relapse after, or relapse or progression during, antiestrogen therapy. This descriptive study analyzed European treatment patterns for HR-positive MBC in real-world clinical practice.

Methods: The IMS Oncology Analyzer (OA), a retrospective cancer treatment database reporting physician-entered patient case histories, was used to identify records for postmenopausal women with HR-positive MBC from April 1, 2004 to June 30, 2013 in France, Germany, Italy, and Spain. Treatments were allocated to mutually exclusive categories (fulvestrant-containing, aromatase inhibitor [AI]-containing, tamoxifen-containing, or chemotherapy-containing regimens) and assessed by line of therapy for MBC. Fulvestrant use was also assessed pre- and post-2010 (when fulvestrant 500 mg dosing was approved).

Results: In total, 27,214 eligible patients were included (France: 6801; Germany: 6852; Italy: 7061; Spain: 6500). Chemotherapy-based regimens were the most common first-line treatments for MBC across all countries. Across countries, the proportion of patients initiating on each treatment category ranged from: chemotherapy, 57.5–70.4%; AI, 23.5–30.1%; tamoxifen, 2.7–9.8%; fulvestrant 0.8–2.6%. When administered, fulvestrant was usually given as first- or second-line treatment. Post-2010, more patients received fulvestrant 500 mg than fulvestrant 250 mg in France, Germany, and Spain; in Italy, more patients continued to receive fulvestrant 250 mg.

Conclusion: Most patients with HR-positive MBC receive chemotherapy over endocrine therapy; fulvestrant constitutes a small proportion of treatments for such patients.

1. Introduction

Breast cancer is one of the most prevalent forms of cancer in the world and the most common cancer among women, with over 1.6 million global cases reported in 2010 [1]. Approximately 80% of all breast cancers are hormone receptor (HR)-positive [2]. Expert consensus guidelines from the European School of Oncology-European Society of Medical Oncology (ESO-ESMO), first published in 2012 [3] and updated in 2014 [4], advise that, even in the presence of asymptomatic visceral metastases, patients with HR-positive, HER2-negative advanced breast cancer should be preferentially treated with endocrine therapy. Due to tolerability issues and the efficacy of endocrine therapies, guidelines recommend that chemotherapy agents should be reserved for patients with rapidly progressing disease or endocrine resistance.

Several endocrine agents are approved and available to treat HR-positive metastatic breast cancer (MBC). The selective estrogen receptor (ER) modulator, tamoxifen, is an antagonist of

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Abbreviations

AI	aromatase inhibitor
ECOG	Eastern Cooperative Oncology Group
EMA	European Medicines Agency
ER	estrogen receptor
ESO-ESMO	European School of Oncology–European Society of Medical Oncology
ET	endocrine therapy
ETS	Enhanced Tumor Studies
HER2	human epidermal growth factor receptor 2
HR	hormone receptor
IHC	immunohistochemistry
MBC	metastatic breast cancer
OA	Oncology Analyzer
OS	overall survival

the ER on ER-positive breast cancer cells. Aromatase inhibitors (AIs) which impede the conversion of circulating androgens to estrogen, such as the non-steroidal AIs anastrozole [5] and letrozole [6] and the steroidal AI exemestane [7], have demonstrated at least equivalent or superior efficacy compared with tamoxifen in the treatment of postmenopausal women with locally advanced breast cancer and/or MBC, with an improved tolerability profile.

Fulvestrant, an ER antagonist with no known agonist effects, suppresses estrogen signaling by binding to and degrading the ER [8,9]. Fulvestrant 250 mg was approved by the European Medicines Agency (EMA) in 2004 for the treatment of postmenopausal women with ER-positive locally advanced breast cancer or MBC for disease relapse on or after adjuvant antiestrogen therapy, or disease progression on therapy with an antiestrogen. Fulvestrant was approved as a monthly 250 mg dosing regimen based on time-to-progression data demonstrating non-inferiority versus anastrozole in postmenopausal women whose advanced breast cancer had progressed during prior antiestrogen therapy [10]. However, early clinical observations, combined with preclinical data suggesting a dose-dependent suppression of ER [11], prompted investigation of fulvestrant treatment at higher doses. The international CONFIRM trial compared fulvestrant 500 mg (fulvestrant 500 mg every month with an additional 500 mg loading dose on Day 14 of the first month) with the monthly 250 mg dose and demonstrated that fulvestrant 500 mg was associated with improved progression-free survival and overall survival (OS) in postmenopausal women with HR-positive advanced breast cancer whose disease had recurred or progressed after prior endocrine therapy [12,13]. As a result of these findings, fulvestrant 500 mg was approved by the EMA in 2010. Recently, an OS benefit for fulvestrant 500 mg compared with anastrozole has been suggested in the first-line treatment of advanced breast cancer [14]. Given the distinct mechanism of action and lack of cross-reactivity of fulvestrant compared with other endocrine therapies [15], fulvestrant would also appear to be a suitable candidate for combination therapy [16].

Real-world evidence studies provide important data on the use of therapies which can be used to compare routine clinical practice with guideline recommendations. Using data from a pan-European clinical database, the aims of this study were to identify treatment patterns by class and line of therapy in routine clinical management of patients with HR-positive MBC, and to assess patterns of fulvestrant use.

2. Methods

2.1. Data source

The data source was Oncology Analyzer (OA; IMS Health, London, UK). OA is a fully syndicated, retrospective, longitudinal cancer treatment database collecting anonymized patient-level oncology data in France, Germany, Italy, Spain, and the UK. The database reports patient case history information relating to the treatment of patients across all cancer types. Physicians in the OA panel contribute data during a 7–28-day period each quarter; for every patient they personally treat in that period (up to a specified cap ranging from 14 to 19 patients per doctor quarterly), the physician completes an OA case report form, using the patient's medical records to produce an individual case history. The OA captures approximately 2–4% of the treated prevalence across cancer types. This process is supplemented by additional data on specific indications and sub-populations such as MBC from the Enhanced Tumor Studies (ETS) database, which requests additional information from a different panel of physicians to OA, with a minimal overlap of physicians permitted. In this manner, approximately 7–10% of the treated prevalence of MBC is covered by this study.

2.2. Study design

This analysis reports treatment patterns for the relevant therapies in routine clinical care in France, Germany, Italy, and Spain. In the OA, patient records are available retrospectively from the date the physician completes the case report form detailing the diagnosis. Each patient record contains information post-diagnosis until the date the case report form is completed. Although no information is available on the patient prior to their diagnosis date, the OA questionnaire captures a range of oncology-relevant information.

2.3. Study population

Postmenopausal (status as recorded in OA) women with HR-positive MBC and a concomitant tumor stage assessment of III or IV were identified during an observation period from April 1, 2004 (immediately post-EMA approval of fulvestrant 250 mg for treatment of breast cancer) to June 30, 2013. Patients could either be diagnosed with MBC, or have been originally diagnosed with primary breast cancer with subsequent metastases, and were required to have received their diagnosis within the specified observation period; the date of diagnosis of metastatic disease was used as the index date. Patients were excluded only if they had participated in a clinical trial evaluating a drug for breast cancer treatment at any time.

2.4. Analyses of treatment patterns

Patient records were subsequently assessed for inclusion in therapy categories using the Anatomical Therapeutic Chemical Classification System, and were allocated to one of four mutually exclusive categories in order of descending priority: fulvestrant-containing regimen; AI-containing regimen; tamoxifen-containing regimen; or chemotherapy-containing regimen (including cyclophosphamide, methotrexate and 5-fluorouracil, anthracyclines, taxanes, trastuzumab, lapatinib, bevacizumab, everolimus, pertuzumab, trastuzumab emtansine, capecitabine, vinorelbine, gemcitabine, eribulin, cisplatin, etoposide, vinblastine, and fluorouracil). As patients receiving human epidermal growth factor receptor 2 (HER2)-targeted therapy were included in this