European Journal of Cancer 94 (2018) 206–215

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Health-related quality of life from the FALCON phase III randomised trial of fulvestrant 500 mg versus anastrozole for hormone receptor-positive advanced breast cancer

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Received 24 November 2017; received in revised form 16 February 2018; accepted 20 February 2018

KEYWORDS
Anastrozole;
FALCON;
Fulvestrant;
Health-related quality of life;
Locally advanced or metastatic breast cancer

Abstract ***Background:*** The phase III randomised FALCON trial (NCT01602380) demonstrated improved progression-free survival with fulvestrant 500 mg versus anastrozole 1 mg in endocrine therapy-naïve postmenopausal women with hormone receptor-positive (HR+) locally advanced or metastatic breast cancer (LA/MBC). Furthermore, overall health-related quality of life (HRQoL) was maintained and comparable for fulvestrant and anastrozole. Here, we present additional analyses of patient-reported HRQoL outcomes from FALCON.

Methods: Women with endocrine therapy-naïve HR+ LA/MBC were randomised 1:1 to fulvestrant (days 0, 14, 28, then every 28 d) or anastrozole (daily) until disease progression or discontinuation. HRQoL was assessed by FACT-B questionnaire (TOI and FACT-B total

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https://doi.org/10.1016/j.ejca.2018.02.026

score) at randomisation and every 12 weeks during treatment. HRQoL data post-treatment (with or without progression) were also collected.
Results: In total, 462 patients were randomised (fulvestrant, n = 230; anastrozole, n = 232). Compliance to FACT-B overall ranged from 60.0 to 97.4%. Mean change from baseline in TOI and FACT-B total score remained broadly stable (approximately ± 3 points to week 132) and was similar between arms during treatment. HRQoL was also maintained in FACT-B subscales. Approximately one-third of patients had improved TOI (≥+6 points) and FACT-B (≥+8 points) total scores from baseline up to week 120 and 132, respectively, of treatment with fulvestrant (ranges 26.4–45.0% and 22.4–35.8%, respectively) and anastrozole (ranges 18.6–32.9%, and 22.7–37.9%, respectively).
Conclusions: Mean change from baseline in TOI and FACT-B total score was maintained for fulvestrant and anastrozole; similar proportions of patients in both arms had improved TOI and FACT-B total scores.
ClinicalTrials.gov identifier: NCT01602380.

1. Introduction

Endocrine monotherapy is the recommended first-line treatment for the majority of postmenopausal patients with hormone receptor-positive (HR+), locally advanced or metastatic breast cancer (LA/MBC) [1–3]. First-line treatment options that are currently recommended include tamoxifen or an aromatase inhibitor (AI), such as anastrozole, letrozole, or exemestane, fulvestrant, and the cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with an AI [1–3]. Fulvestrant is a selective oestrogen-receptor degrader that blocks oestrogen-receptor function [4] and was originally approved by the European Medicines Agency for the treatment of postmenopausal patients with HR+ LA/MBC, and by the United States Food and Drug Administration for postmenopausal women with HR+ MBC, who have progressed on prior anti-oestrogen therapy [5,6]. Fulvestrant is also approved in the USA and Europe for the treatment of patients with HR+ human epidermal growth factor 2-negative advanced or MBC in combination with palbociclib, and in the USA with abemaciclib, following disease progression on prior endocrine therapy [6].

In the double-blind, randomised phase III Fulvestrant and Anastrozole Compared in Hormonal Therapy Naïve Advanced Breast Cancer (FALCON) trial (NCT01602380), fulvestrant 500 mg demonstrated significantly improved progression-free survival (PFS) versus anastrozole 1 mg in postmenopausal women with HR+ LA/MBC who had not received prior endocrine therapy (hazard ratio [HR] = 0.797; 95% confidence interval [CI]: 0.637–0.999; $P = 0.0486$) [7]. These data confirmed the results of the phase II, randomised, open-label FIRST (Fulvestrant First-Line Study Comparing Endocrine Treatments) study (NCT00274469), which reported that fulvestrant 500 mg improved time to disease progression and overall survival compared with anastrozole 1 mg for the first-line treatment of postmenopausal women with HR+ LA/MBC [8–10].

Following these findings, fulvestrant received regulatory approval in Europe, Russia, Japan and the USA for the first-line treatment of postmenopausal women with LA/MBC.

In addition to delaying progression and prolonging survival, a further aim of treatment for HR+ LA/MBC is to optimise health-related quality of life (HRQoL) [1,2]. HRQoL outcomes are now considered to be important end-points in cancer clinical trials [11,12]. Indeed, consideration of HRQoL for patients with LA/MBC is recommended in treatment guidelines [1,2] and may support regulatory submissions [13,14]. This is particularly relevant considering the approval of fulvestrant as a combination therapy with palbociclib [6] and abemaciclib [15], as patients with MBC may receive multiple therapies, potentially affecting adverse event (AE) profiles and HRQoL. Furthermore, given that HRQoL can be a prognostic indicator, it is important that clinicians consider HRQoL in clinical decision-making [16].

HRQoL with fulvestrant has previously been evaluated in the second-line setting. Results of the phase III, randomised, double-blind Comparison of Faslodex in Recurrent or Metastatic Breast Cancer (CONFIRM) study that compared fulvestrant 250 and 500 mg demonstrated that no significant difference in HRQoL was detected between the two study arms, as determined by the Functional Assessment of Cancer Therapy for Breast Cancer (FACT-B)-derived Trial Outcome Index (TOI) [17]. In the second-line PALOMA-3 study, global HRQoL scores and improvement from baseline in pain were significantly improved with fulvestrant plus palbociclib versus fulvestrant plus placebo. No significant differences were reported for the European Organisation for Research and