Phase III Trial Shows Improved Progression-Free Survival With Fulvestrant vs Anastrozole in Advanced Breast Cancer

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In the international phase III FALCON trial, reported in *The Lancet*, **John F.R. Robertson, MD**, of the University of Nottingham, United Kingdom, and colleagues found that progression-free survival was improved with intramuscular fulvestrant (Faslodex) vs oral anastrozole in endocrine therapy–naive women with hormone receptor (HR)-positive locally advanced or metastatic breast cancer.[1]

Study Details

In the double-blind trial, 462 patients from 113 sites in 20 countries in Asia, Europe, North America, South America, and South Africa were randomly assigned between October 2012 and July 2014 to receive fulvestrant (n = 230) or anastrozole (n = 232). Fulvestrant was given as 500-mg intramuscular injections on days 0, 14, 28, and every 28 days thereafter; anastrozole was given at 1 mg orally daily. The primary endpoint was progression-free survival in the intent-to-treat population.

For the fulvestrant and anastrozole groups, median age was 64 and 62 years (47% and 39% ≥ 65 years); 76% and 75% were white, and 16% and 15% were Asian; time from diagnosis was ≥ 1 year for 30% and 29%; 76% and 77% were estrogen receptor– and progesterone receptor

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> *— John F.R. Robertson, MD, and colleagues*

–positive; 88% and 86% had metastatic disease; 59% and 51% had visceral disease; 84% and 84% had measureable disease;16% and 19% had received chemotherapy for locally advanced or metastatic disease; and 23% and 22% had received radiotherapy.

Progression-Free Survival

Median progression-free survival was 16.6 months (95% confidence interval [CI] = 13.83–20.99 months) in the fulvestrant group vs 13.8 months (95% CI = 11.99–16.59 months) in the anastrozole group (hazard ratio [HR] = 0.797, (95% CI = 11.99 –16.59 months) in the anastrozole group (hazard ratio [HR] = 0.797, 95% CI = 0.637–0.999, *P* = .0486). Among patients with measurable disease, an objective response was observed in 46% (89/193) of fulvestrant recipients and 45% (88/196) of anastrozole recipients (odds ratio = 1.07, 95% CI = 0.72–1.61, *P* = .7290); the median duration of response was 20.0 (95% CI = 15.90–27.63) vs 13.2 (95% CI = 10.64–16.72) months.

Hormone Therapy in Advanced Breast Cancer

- Fulvestrant improved progression-free survival vs anastrozole among patients with no prior endocrine therapy.
- The benefit of fulvestrant vs anastrozole was more marked in patients with nonvisceral disease.

The magnitude of progression-free survival benefit with fulvestrant was consistent across most prespecified subgroups, except for patients with previous chemotherapy for locally advanced or metastatic disease, patients with nonmeasurable disease, patients who were not estrogen receptor– and progesterone receptor –positive, and patients with visceral disease. For example, hazard ratios were 0.59 (95% CI = 0.42 –0.84; median progression-free survival = 22.3 [95% CI = 16.62–32.79] vs 13.8 months [95% CI = 11.04–16.59]) among patients with nonvisceral disease and 0.99 (95% CI = 0.74–1.33; median progression-free survival = 13.8 [95% CI = 11.04–16.53] vs 15.9 [95% CI = 11.27–16.89]) among those with visceral disease (post hoc interaction test *P* = .0092).

Median overall survival could not yet be calculated. At data cutoff, death had occurred in 29% of the fulvestrant group vs 32% of the anastrozole group (HR = 0.88, 95% CI = 0.63–1.22, *P* = .4277).

Adverse Events

The most common adverse events of any grade were arthralgia (17% in fulvestrant group vs 10% in anastrozole group) and hot flushes (11% vs 10%). Grade ≥ 3 adverse events occurred in 22% vs 18%. Serious adverse events occurred in 13% vs 13%. Adverse events of special interest—ie, joint disorders and back pain—occurred in 26% vs 18%. Adverse events led to discontinuation of treatment in 7% vs 5%. A total of 3% of patients in each group died, but none of the deaths were considered to be related to study treatment.

The authors concluded: "Fulvestrant has superior efficacy and is a preferred treatment option for patients with hormone receptor–positive locally advanced or metastatic breast cancer who have not received previous endocrine therapy compared with a third-generation aromatase inhibitor, a standard of care for first-line treatment of these patients." ■

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Reference

1. Robertson JF, Bondarenko IM, Trishkina E, et al: Fulvestrant 500 mg versus anastrozole 1 mg for hormone receptor-positive advanced breast cancer (FALCON): An international, randomised, double-blind, phase 3 trial. Lancet 388:2997-3005, 2016.

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