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Extended therapy with letrozole as adjuvant treatment of postmenopausal patients with early-stage breast cancer: A randomised, phase III trial of the Gruppo Italiano Mammella

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Background

The benefit of extended adjuvant therapy with aromatase inhibitors (AIs) in postmenopausal hormone-receptor positive breast cancer patients treated with tamoxifen for 2-3 years followed by an AI for 2-3 years is still controversial. We aimed to determine whether, after 2-3 years of tamoxifen, 5 years of letrozole is more effective than the standard duration of 2-3 years.

Methods

This is a prospective, open-label, phase 3 trial conducted in 64 Italian hospitals within the Gruppo Italiano Mammella (GIM). Stage I-III breast cancer patients, free of recurrence after 2-3 years of tamoxifen, were randomly allocated (1:1) with a centralized, interactive online system to receive 2-3 years (control arm) or 5 years (extended arm) of letrozole. Primary endpoint was disease-free survival (DFS) in the intention-to-treat population. Overall survival (OS) and safety were secondary endpoints.

Results

Between August 1, 2005, and October 24, 2010, we recruited 2056 patients. After a median follow-up of 11.7 years (IQR 9.5-13.1), 262 (25%) of 1030 patients in the control arm and 212 (21%) of 1026 patients in the extended arm experienced a DFS event. The 12-year DFS was 62% (95% CI 57-66) and 67% (62-71) in the control and extended arm, respectively (Hazard Ratio [HR] 0.78, 0.65-0.93; $p=0.006$). The effect did not change in a multivariate Cox model including nodal status, tumor size, grading, age, hormone receptor status, HER2 status, previous chemotherapy, and BMI ($p=0.014$). Overall, 263 (13%) deaths occurred, 147 in the control arm and 116 in the extended arm. The 12-year OS was 84% (82-87) in the control arm and 88% (86-90) in the extended arm (HR 0.77, 0.60-0.98; $p=0.036$). Arthralgia (31% vs 38%), myalgia (8% vs 12%), hypertension (1% vs 2%) and osteoporosis (5% vs 8%) were significantly more frequent in the experimental arm.

Conclusions

In post-menopausal breast cancer patients treated with 2-3 years of tamoxifen, extended treatment with 5 years of letrozole resulted in a significant and clinically meaningful improvement in both DFS and OS compared to the duration of 2-3 years of letrozole.

Clinical trial identification

EudraCT 2005-001212-44, NCT01064635.

Legal entity responsible for the study

The authors.

Funding

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Disclosure

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