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## Final analysis of the GIM3 FATA trial: Treatment schedule and three aromatase inhibitors (AIs) comparison in postmenopausal HR-positive (HR+) early breast cancer (eBC)

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### Background

Adjuvant AI therapy is standard for postmenopausal women with HR+ eBC. The optimal schedule [upfront vs sequential AI use after tamoxifen (T)] and the relative efficacy of the three third-generation AIs: anastrozole (A), exemestane (E), letrozole (L) remain unresolved. GIM3 FATA is the only randomized trial prospectively powered to address both questions in parallel, fully investigator-initiated and academically funded.

### Methods

Postmenopausal women with HR+ eBC were randomly assigned 1:1:1:1:1 to 5 years of A, E, or L, given upfront or after 2 years of T. Co-primary endpoints were disease-free survival (DFS) for upfront vs switch and DFS across the three AIs. Secondary endpoints included overall survival (OS), distant DFS, distant relapse-free survival, relapse-free survival, and breast cancer-free interval, analyzed under updated STEEP 2.0 criteria.

### Results

Between March 2007 and July 2012, 3697 patients were enrolled at 76 Italian centers; median age was 64 years. At a median follow-up of 88.9 months, 796 DFS (792 required) events and 491 deaths had occurred. For upfront vs switch there was no statistically significant difference for DFS (HR 0.95, 95% CI 0.82-1.09) and OS (HR 0.88, 95% CI 0.74-1.06). The 10-year DFS was 79.1% (95% CI 76.1-81.7) with A, 74.2% (95% CI 70.9-77.2) with E, and 76.6% (95% CI 73.3-79.5) with L (global log-rank p=0.028; pairwise comparison: E vs A statistically significant p=0.010, E vs L p=0.06, L vs A p=0.51). In the adjusted Cox model stratified by treatment schedule, the HR for DFS for E vs A was 1.23 (95% CI 1.04-1.46). 10-year OS was not different among A, E and L (global log-rank p=0.25). Toxicity differed by schedule (more musculoskeletal events with upfront; more T-related events with switch) and by AI (more hypercholesterolemia with non-steroidal AIs).

### Conclusions

No schedule was superior, but E was associated with worse DFS. Schedule and AI choice should be individualized by tolerability and comorbidities. Pharmaco-economic considerations are advised since both E and L are nearly twice as expensive as A in most countries.

### Clinical trial identification

This trial is registered with the European Clinical Trials Database, number 2006-004018-42, NCT00541086.

### Legal entity responsible for the study

Oncotech Consortium.

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**Disclosure**

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