Fulvestrant plus anastrozole for metastatic breast cancer

Adding fulvestrant to anastrozole improves overall survival in patients with metastatic hormone receptor-positive breast cancer compared with anastrozole alone, according to an updated analysis of the S0226 trial.

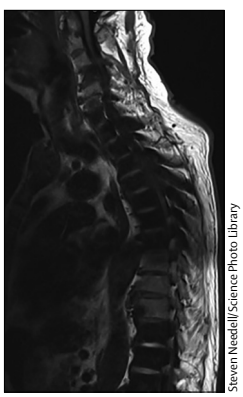
Rita S Mehta (Chao Family Comprehensive Cancer Center, University of California Irvine Medical Center, Orange, CA, USA) and colleagues did a multicentre, phase 3 trial in postmenopausal women with metastatic breast cancer, who were randomly assigned to receive either anastrozole (n=345) or anastrozole plus fulvestrant (n=349). Eligible patients had oestrogen-receptor–positive or progesterone-receptor–positive metastatic breast cancer, a Zubrod's performance-status score of 0 to 2, and had not previously received chemotherapy, hormonal therapy, or immunotherapy for metastatic disease. Crossover to the combination therapy group was encouraged for patients in the anastrozole group who had disease progression. The primary endpoint was progression-free survival. Results from the primary analysis were previously published.

Here the authors report the final analysis of overall survival. At a median follow-up of 7 years, 247 (71%) of 349 women in the combination therapy group and 261 (76%) of 345 women in the anastrozole-alone group had died. Median overall survival was 49·8 months in the combination therapy group compared with 42·0 months in the anastrozole-alone group (hazard ratio [HR] 0·82 [95% CI 0·69–0·98]; p=0·03). Subgroup analysis in patients who did not receive previous tamoxifen showed a median overall survival of 52·2 months in the combination therapy group compared with 40·3 months in the anastrozole-alone group (HR 0·73 [95% CI 0·58–0·92]). 45% of patients in the anastrozole-alone group crossed over to receive fulvestrant.

"The combination therapy comes without major side-effects such as hair loss, fatigue, or infection", explained Mehta.

Sanjeev Kumar (Cancer Research UK Cambridge Institute and University of Cambridge, Cambridge, UK) welcomed the results but cautioned that the study was done in a selected patient population: women with metastatic disease who have not been heavily pretreated. "It would be good to see a study comparing fulvestrant plus anastrozole with a CDK4–6 inhibitor plus an aromatase inhibitor, so that we can identify which is the better first-line treatment, particularly given the more favourable toxicity profile of anastrozole plus fulvestrant," he told *The Lancet Oncology*.

Talha Khan Burki



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For the **study by Mehta and colleagues** see *N Engl J Med* 2019; **380:** 1226–34

For the **primary analysis** see *N Engl J Med* 2012; **367:** 435–44