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Final analysis of NRG oncology/NSABP B-42, a randomized, double-blinded, placebo-controlled trial of extended letrozole in postmenopausal women with hormone-receptor positive breast cancer who have completed previous adjuvant therapy with an aromatase inhibitor

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Background

NSABP B-42 evaluated whether 5 yrs of letrozole (L) vs placebo (P) improves disease-free survival (DFS) in patients who received 5 yrs of endocrine therapy. Previous 10-yr results showed that L significantly improved the primary endpoint of DFS and secondary endpoints of breast cancer-free interval (BCFI) and distant recurrence (DR) with no significant improvement in overall survival (OS). Here we report the final trial analysis of 15-yr outcome data.

Methods

A total of 3,966 postmenopausal patients with stage I-III, hormone-receptor positive breast cancer, disease-free after 5 yrs of an aromatase inhibitor (AI) or ≤ 3 yrs of tamoxifen $\rightarrow$ AI for total of 5 yrs, were randomized 1:1 to 5 yrs of L 2.5 mg PO daily or P. Stratification was by pathologic nodal status, prior tamoxifen or not, and baseline DEXA T scores (> -2.0 , ≤ -2.0 SD). Primary endpoint was DFS. Secondary endpoints included OS, BCFI and DR. Differences in outcomes between L and P were assessed by stratified log-rank tests and Cox proportional hazards models.

Results

Follow-up of trial patients was completed in 08/26, with median follow-up of 15.9 yrs. Since the 10-yr update, 538 additional DFS events were recorded. The 15-yr results continue to show a modest but significant improvement in DFS (HR=0.85, 95%CI=0.77 to 0.94, 15-yr DFS: P=56.5%, L=61.6%), BCFI (HR=0.78, 95%CI=0.67 to 0.92, 15-yr BCFI risk: P=18.3%, L=14.7%) and DR (HR=0.72, 95%CI=0.57 to 0.91, 15-yr DR risk: P=9.7%, L=6.9%). The L effect on DFS was consistent across subgroups by stratification factors. There was no significant improvement in OS (HR=0.92, 95%CI=0.82 to 1.05, 15-yr OS: P=72.3%, L=74.0%).

Conclusions

With over 15 yrs of follow-up, the B-42 trial continues to demonstrate a sustained and clinically meaningful benefit with extended letrozole therapy on DFS and key secondary endpoints consistent with the original and 10-yr updated results. No attenuation of treatment effect was observed from year 10 to year 15.

Clinical trial identification

NCT00382070.

Legal entity responsible for the study

NRG Oncology/NSABP Foundation Inc.

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Disclosure

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