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LETTER

Are another 5 years of adjuvant aromatase inhibitor therapy needed?

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Dear editor

In the recent issue of *Breast Cancer: Targets and Therapy*, some questions about adjuvant systemic therapy[1] and bone loss and skeletal-related events in postmenopausal women with hormone receptor-positive breast cancer[2] were discussed by two reviews.

We are concerned about the content of adjuvant endocrine therapy for postmenopausal women who have hormone receptor-positive early breast cancer. Guidelines recommended a minimum of 5 years of adjuvant therapy with an aromatase inhibitor or tamoxifen followed by an aromatase inhibitor (in either order) for such patients.[3–5] However, the safety and efficacy of extending treatment with an aromatase inhibitor for another 5 years are unknown.

Recently, Goss et al[6] reported results from the MA.17R trial in favor of extending the use of adjuvant aromatase inhibitor therapy for another 5 years in such patients. Women receiving such therapy showed significantly higher disease-free survival and lower incidence of contralateral breast cancer than women on placebo for the same period. On the basis of these findings, Goss et al[6] recommended extending letrozole therapy for another 5 years.

As stated by these two reviews[1,2] and another review,[7] such a recommendation should be counterbalanced against the possibility that, for many patients, prolonging letrozole therapy may provide no benefit or may, in fact, cause more harm than good. In the study by Goss et al,[6] the overall survival at 5 years was similar between patients receiving letrozole or placebo for another 5 years (P=0.83) and the two groups were similar on most of the quality-of-life measures applied. The two groups also had no significant differences in any of the prespecified subgroups. More importantly, bone-related toxic events, including bone pain, fracture, and new-onset osteoporosis, were significantly more common in the letrozole group than in the placebo group.

Only ~3% of patients in each arm of the study died from breast cancer-related recurrence, suggesting that the cohort may have passed the peak of tumor recurrence risk, perhaps in part because they had already undergone 4.5–6.0 years of adjuvant aromatase inhibitor therapy. In addition, the best we know for now is that young patients may die from tumor recurrence, while old patients may die just from age.[7] Indeed, the participants in the study self-selected for the trial and likely represent patients who experienced fewer minor side effects during previous aromatase inhibitor therapy. It is possible that they underestimate the toxicity associated with another 5 years of letrozole therapy in the broader target population.

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Given these concerns as well as the cost of aromatase inhibitor therapy, we urge the clinical community to view the results from trials in a wider perspective when conducting cost–benefit analyses to decide whether to extend letrozole therapy. Therefore, the decision to prolong therapy should be carefully considered for each patient.

Disclosure

The authors report no conflicts of interest in this communication.

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Authors' reply

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Dear editor

We read the letter from Mo et al with great interest. With respect, we deeply regret that the authors did not read the content of our review in detail. They raised the concern that our manuscript supports or suggests in any way the use of aromatase inhibitors for 5 additional years after the initial 5 years of therapy. This is inaccurate, as our manuscript does not mention this. In our manuscript, we described: "Current data supports the use of aromatase inhibitors for at least 5 years. Ongoing trials are evaluating the benefit of continuing therapy beyond 5 years."[1]

In addition to the misinterpretation of our manuscript content, we regret that the authors of the letter did not put our review in the context of available data at the time of its publication. They went on to describe in their letter the results of the MA.17R trial. It is worth noting that the results of this trial were first reported on June 5, 2016, during the plenary session of ASCO Annual Meeting,[2] and our manuscript was accepted for publication on May 24, 2016. At the time we wrote our review article, we had no knowledge of the MA.17R results.

Disclosure

The authors report no conflicts of interest in this communication.

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