

Are another 5 years of adjuvant aromatase inhibitor therapy needed?

Qin-Guo Mo*
De-Quan Li*
Jian-Hong Zhong
Chang-Yuan Wei

Department of Breast Surgery,
Affiliated Tumor Hospital of Guangxi
Medical University, Nanning, People's
Republic of China

*These authors contributed equally to
this work

Dear editor

In the recent issue of *Breast Cancer: Targets and Therapy*, some questions about adjuvant systemic therapy¹ and bone loss and skeletal-related events in postmenopausal women with hormone receptor-positive breast cancer² 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 al⁶ 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 al⁶ 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.

Correspondence: Chang-Yuan Wei
Department of Breast Surgery, Affiliated
Tumor Hospital of Guangxi Medical
University, Hedi Road, No 71, Nanning
530021, People's Republic of China
Tel +86 771 533 0855
Fax +86 771 531 2000
Email weicy63@aliyun.com

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.

References

1. Leone J, Leone BA, Leone JP. Adjuvant systemic therapy in older women with breast cancer. *Breast Cancer (Dove Med Press)*. 2016;8:141–147.
2. Yardley DA. Pharmacologic management of bone-related complications and bone metastases in postmenopausal women with hormone receptor-positive breast cancer. *Breast Cancer (Dove Med Press)*. 2016;8:73–82.
3. Burstein HJ, Lacchetti C, Anderson H, et al. Adjuvant endocrine therapy for women with hormone receptor-positive breast cancer: American Society of Clinical Oncology Clinical Practice Guideline Update on Ovarian Suppression. *J Clin Oncol*. 2016;34(14):1689–1701.
4. Burstein HJ, Temin S, Anderson H, et al. Adjuvant endocrine therapy for women with hormone receptor-positive breast cancer: American Society of Clinical Oncology Clinical Practice Guideline Focused Update. *J Clin Oncol*. 2014;32(21):2255–2269.
5. National Comprehensive Cancer Network (NCCN). *NCCN Clinical Practice Guidelines in Oncology. Breast Cancer. Version 2.2016*. Available from: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed October 25, 2016.
6. Goss PE, Ingle JN, Pritchard KI, et al. Extending aromatase-inhibitor adjuvant therapy to 10 years. *N Engl J Med*. 2016;375(3):209–219.
7. Jerzak KJ, Desautels DN, Pritchard KI. An update on adjuvant systemic therapy for elderly patients with early breast cancer. *Expert Opin Pharmacother*. 2016;17(14):1881–1888.

Authors' reply

Julieta Leone¹

Bernardo Amadeo Leone¹

José Pablo Leone²

¹Department of Medical Oncology, Grupo Oncológico Cooperativo del Sur, Neuquén, Argentina; ²Division of Hematology-Oncology and Blood & Marrow Transplantation, Department of Internal Medicine, University of Iowa Holden Comprehensive Cancer Center, University of Iowa Hospitals and Clinics, Iowa City, IA, USA

Correspondence: José Pablo Leone
Division of Hematology-Oncology and Blood & Marrow Transplantation, Department of Internal Medicine, University of Iowa Holden Comprehensive Cancer Center, University of Iowa Hospitals and Clinics, 200 Hawkins Drive, C32 GH Iowa City, IA 52242-1081, USA
Tel +1 319 356 7839
Fax +1 319 353 8383
Email jose-leone@uiowa.edu

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.

References

1. Leone J, Leone BA, Leone JP. Adjuvant systemic therapy in older women with breast cancer. *Breast Cancer*. 2016;8:141-147.
2. Goss PE, Ingle JN, Pritchard KI, et al. Extending aromatase-inhibitor adjuvant therapy to 10 years. *N Engl J Med*. 2016;375(3):209-219.

Dove Medical Press encourages responsible, free and frank academic debate. The content of the Breast Cancer: Targets and Therapy 'letters to the editor' section does not necessarily represent the views of Dove Medical Press, its officers, agents, employees, related entities or the Breast Cancer: Targets and Therapy editors. While all reasonable steps have been taken to confirm the content of each letter, Dove Medical Press accepts no liability in respect of the content of any letter, nor is it responsible for the content and accuracy of any letter to the editor.

Breast Cancer - Targets and Therapy

Publish your work in this journal

Breast Cancer - Targets and Therapy is an international, peer-reviewed open access journal focusing on breast cancer research, identification of therapeutic targets and the optimal use of preventative and integrated treatment interventions to achieve improved outcomes, enhanced survival and quality of life for the cancer patient.

Submit your manuscript here: <https://www.dovepress.com/breast-cancer---targets-and-therapy-journal>

Dovepress

The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.