

# Comparative study on individual aromatase inhibitors on cardiovascular safety profile: misleading analysis and doubtful methodology

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## Dear editor

Zhao et al have presented the result of the relative cardiovascular safety profile in using anastrozole, letrozole, and exemestane to treat the postmenopausal estrogen receptor-positive breast cancer, in which fatal or nonfatal myocardial infarction is the outcome measure and ten randomized controlled trials are used as the data sources.<sup>1</sup> We congratulate and applaud their important work, but there are some issues of concern.

First, the difference in duration of adjuvant tamoxifen therapy among the studies led to heterogeneity and inconsistency. For instance, the duration of tamoxifen therapy was 2 years in the TEAM (Tamoxifen Exemestane Adjuvant Multinational) trial, whereas it was 5 years in the ATAC (Arimidex, Tamoxifen, Alone or in Combination) trial. In fact, the duration of tamoxifen therapy is relevant to toxicity. The practice of “lumping” cotreatments together generally makes no sense in clinical practice.<sup>2</sup> In addition, the author regarded the sequential therapy (tamoxifen for 2 years followed by anastrozole for 3 years) or the extended adjuvant therapy (tamoxifen for 5 years followed by anastrozole for 3 years) as the anastrozole group, which was misleading. In fact, the tamoxifen would have the “crossover” effect even after the completion of the 2-, 3-, or 5-year treatment period. Instead, the author should have considered comparing the safety profile among the initial aromatase inhibitor therapy, sequential therapy, and extended therapy, which would be of a more meaningful clinical significance.

Second, the authors failed to include three relevant randomized controlled trials in their meta-analysis, although they apparently met their inclusion criteria.<sup>3-5</sup>

Third, there was one important methodological issue in this review. The reporting of the inconsistency between the direct and indirect comparison is laudable in a network meta-analysis. However, this review did not describe the methodology of the inconsistency analysis in the “Statistical analysis” section.

Finally, in Figure 3, it was described that both severe and total cardiovascular risk deviance information criterion values were  $<200$ , which means that the calculated results were convincing. We are interested in the source of this perspective. In addition, the methodology of model fit was not confirmed in the “Statistical analysis” section.

## Disclosure

The authors report no conflicts of interest in this communication.

## References

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