Reviewer's report

Title: Safety and survival effect comparison of adjuvant tamoxifen and toremifene in premenopausal patients with ER/PR positive breast cancer: a retrospective cohort study

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Reviewer: Rupert Bartsch

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Safety and survival effect comparisons of adjuvant tamoxifen and toremifene in premenopausal patients with ER/PR positive breast cancer: a retrospective cohort study

Ran Gul et al.

Authors report that toremifene as adjuvant therapy for early breast cancer in premenopausal women may offer a benefit in terms of progression-free survival as compared to tamoxifen.

The manuscript, while interesting, has a number of fundamental problems which need to be addressed.

1. How were the cohorts defined? In other words, who decided which patient will receive toremifene or tamoxifen? On what basis was the decision made?
2. Authors apparently defined premenopausal simply by age ≤50. Are there any data concerning hormone levels? This needs to be resolved! In the discussion section, it is stated that E2 and FSH levels were monitored!
3. Was a sample-size calculation performed?
4. Authors state in the methods section that all patients with >3 axillary lymph nodes received radiotherapy independent of breast conservation or mastectomy. Does that mean that not all patients treated with breast conservation were irradiated? Again, this is crucial as there was an imbalance in the local control between the two groups. In other words, all outcome differences may be simply explained by radiotherapy.
5. What chemotherapeutic regimens were used? Was there any difference in the use of taxanes? Was there any difference in duration or intensity of chemotherapy?
6. Was the any difference in the proportion of patients who discontinued treatment between the two groups?
7. Authors use word such as “assigned to” “accrue” or “prospective follow up” which would rather fit a prospective study. On the other hand, the manuscript is called “a retrospective cohort study”
8. In introduction section of the abstract, I would rather state that endocrine therapy for premenopausal women consists of tamoxifen and/or ovarian
suppression.

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.