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Letter

Reply to comment on "Anastrozole (Arimidex ™) versus tamoxifen as first-line therapy for advanced breast cancer in postmenopausal women: survival analysis and updated safety results" by H.T. Mouridsen, H.A. Chaudri-Ross☆

Mouridsen and colleagues highlight some specific aspects of our manuscript [1], where we had considered our data in the context of a similar study comparing letrozole with tamoxifen as first-line endocrine therapy of advanced breast cancer [2]. One criticism is that we did not quote the complete analysis of this study; however, at the time of our manuscript submission the data were available only in abstract form. However, we would suggest that access to this 'complete analysis' would not have affected our interpretation, since the analysis of overall survival (the primary endpoint) is unchanged, showing no statistically significant difference between letrozole and tamoxifen. Presumably, Mouridsen and colleagues are keen to highlight the proposed 'early survival benefit' they suggest is seen with letrozole. We would like to point out that this exploratory analysis does not reflect the protocolled endpoint of the study and had no relevance to the final outcome for patients.

Mouridsen and colleagues also state that the lower numbers of patients crossing over to the other agent in our trial would make differences in 'early survival' easier to detect. However, we did not analyse survival earlier than 2 years as it was considered to be statistically inappropriate. Furthermore, the lower percentage of patients crossing over has no relevance to the detection of 'early survival,' as patients who did not cross-over went on to receive alternative therapies, which would also have affected the long-term outcome.

The validity of data comparisons across studies is rightly questioned by Mouridsen and colleagues. However, it is standard practice to compare results with those from similar studies in order to help determine their significance. Having said that, we agree that there are likely to be differences between the two studies that restrict the ability to draw firm conclusions about the relative benefits of each agent. For example, the performance of tamoxifen in the letrozole study was unusually poor—a point that has previously been highlighted elsewhere [3]. There are also likely to be additional confounding factors other than those discussed by Mouridsen and colleagues that may influence any such comparisons, e.g. the proportion of patients with tumours of unknown hormone receptor status that were actually hormone receptor-positive. A comparative trial of anastrozole and letrozole will be the only setting in which these two agents can be compared directly.

Lastly, although letrozole showed an advantage over tamoxifen in terms of time to progression, we do not agree that the letrozole survival data are able to support the statement that it is the only aromatase inhibitor with 'proven significantly greater efficacy' over tamoxifen in the first-line treatment of advanced breast cancer. It would be useful to have confirmatory survival data from patients without prior adjuvant or subsequent endocrine therapy. Indeed, data demonstrating a mature survival benefit for anastrozole over tamoxifen are available from an independent comparative study ($n = 238$) in endocrine therapy-naïve patients with oestrogen receptor-positive tumours who received only palliative care once they had progressed on trial therapy [4].

References

1. Nabholtz JM, Bonneterre J, Buzdar A, *et al*. Anastrozole versus tamoxifen as first-line therapy for advanced breast cancer in postmenopausal women: survival analysis and updated safety results. *Eur J Cancer* 2003, **39**, 1684–1689.
2. Mouridsen H, Gershanovich M, Sun Y, *et al*. Phase III study of letrozole versus tamoxifen as first-line therapy of advanced breast cancer in postmenopausal women: analysis of survival and update of efficacy from the International Letrozole Breast Cancer Group. *J Clin Oncol* 2003, **21**, 2101–2109.
3. Buzdar AU. Superior efficacy of letrozole versus tamoxifen as first-line therapy. *J Clin Oncol* 2002, **20**, 876–878.
4. Milla Santos A, Milla L, Portella J, *et al*. Anastrozole versus tamoxifen as first-line therapy in postmenopausal patients with hormone-dependent advanced breast cancer: a prospective, randomized Phase III study. *Am J Clin Oncol* 2003, **26**, 317–322.

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