Editorial

Neoadjuvant treatment for male breast cancer

Ian Stuart Fentiman^

GKT School of Cancer & Pharmaceutical Sciences, Guy's Hospital, London, UK

Correspondence to: Ian Stuart Fentiman, MD, DSc, FRCS. Emeritus Professor of Surgical Oncology, GKT School of Cancer & Pharmaceutical Sciences, Guy's Hospital, London SE1 9RT, UK. Email: Ian.Fentiman@kcl.ac.uk.

Comment on: Chen W, Wang H, Yang B, *et al.* Nomogram for predicting preoperative axillary lymph node status in male breast carcinoma: a SEER population-based study. Transl Cancer Res 2023;12:793-803.

Keywords: Male breast cancer (MBC); neoadjuvant; chemotherapy; endocrine therapy; nomogram

Submitted Apr 04, 2023. Accepted for publication May 30, 2023. Published online Jun 15, 2023.
doi: 10.21037/tcr-23-592
View this article at: https://dx.doi.org/10.21037/tcr-23-592

Unfortunately, a substantial proportion of men present with large, locally advanced or metastatic breast cancer (1,2). Such individuals are best served with neoadjuvant systemic therapy in order to downsize the tumour and render it operable and if possible, enable breast conserving therapy. Sentinel node biopsy (SNB) is the standard approach to staging the clinically negative axilla. Chen *et al.* have conducted an important investigation to develop a nomogram for prediction of SNB status, based on clinico-pathologic variables (3).

Using the Surveillance Epidemiology and End Results (SEER) database of male breast cancer (MBC) registered in 2010-2018 they extracted a cohort of 2610 non-metastatic cases divided 2:1 into a training group (n=1,740) and a validation set (n=870). In a multivariate analysis, it emerged that patient age, tumor stage, location and grade were independent predictive factors of sentinel node metastasis. For the validation group the area under the curve was 0.848, indicating that the nomogram has prognostic value.

This is encouraging but the question has to be asked "Why chemotherapy rather than endocrine therapy?" MBC patients almost invariably have estrogen receptor positive (ER+) disease (4). Endocrine effects may be slower than those from chemotherapy but treatment is less costly and associated with a lower profile of side-effects. Because of similarities in prognostic factors, age-specific incidence and age-frequency distributions, Anderson *et al.* postulated that MBC may be akin to post-menopausal female breast cancer (FBC) (5).

Tamoxifen was regarded as the standard endocrine treatment for post-menopausal FBC treatment until randomized controlled trials (RCTs) showed the superiority of aromatase inhibitors (AIs) (6). This is where the similarity ceases. Harlan *et al.* reported 512 MBC cases from the SEER database and confirmed a significant reduction in cancer mortality with tamoxifen (HR: 0.04) but no impact of adjuvant AIs (HR: 1.2) (7). Furthermore, in a matched comparison of 257 MBC patients with 2785 FBC cases, Eggemann *et al.* reported similar 5-year overall survival (OS) for both genders given tamoxifen but significantly better 5-year OS in females given AIs (85% versus 73.3%) (8). One possible explanation is that gonadal estrogen synthesis is not abolished by AIs. This indicates that Tamoxifen should probably be the neoadjuvant endocrine therapy of choice in MBC with any potential compliance problems being minimised by giving it for only 4 months.

There are gender differences in compliance with tamoxifen therapy so that males are less likely to accept side effects than females. In a report of 24 MBC cases from the Sloane-Kettering Memorial Hospital, receiving adjuvant tamoxifen 15 (63%) complained of side effects including reduced libido (29%), weight gain (25%), hot flushes (21%) and mood alterations in 21% (9). As a result, 21% of males stopped tamoxifen within a year of diagnosis, compared with only 10% of females.

In another study from the Ottawa Hospital Cancer

^ ORCID: 0000-0001-9467-5233.

Centre of 30 MBC cases given tamoxifen, side-effects were reported by 50% while 24% discontinued treatment (10). Similar results were reported from the MD Anderson Cancer Center where 64 MBC patients received adjuvant tamoxifen with 34 (53%) complaining of side-effects (11).

Non-compliance impacts significantly on survival. In a cohort of 116 MBC patients advised a 5-year course of tamoxifen, after 1 year only 75 (65%) were compliant (12). After 2 years compliance fell to 46%, and by the final year only 18% were taking tamoxifen. The 10-year (OS) for compliant patients was 80% compared with only 50% for the non-compliant cases.

Another potential agent is the gonadotropin releasing hormone (GnRH) analogue goserelin, which has been used extensively in the treatment of advanced prostate cancer and has been shown to be well-tolerated (13). There is however scant evidence of use of goserelin in MBC cases. Abdel Azim *et al.* reported a 56-year-old male with bone metastases who achieved a year-long remission with goserelin monotherapy albeit with side-effects including grade II hot flushes and sexual dysfunction (14). Di Lauro *et al.* treated 36 men with metastatic breast cancer using cyproterone acetate with or without goserelin (15). One case who received the combination had a complete remission.

Based on the efficacy in prostate cancer, goserelin could be tested in a randomised trial of neoadjuvant endocrine therapy with MBC patients receiving either goserelin plus tamoxifen or goserelin plus placebo. To conduct such a study would require a multicenter international appropriately powered randomised trial including quality of life metrics. Collaboration has started with pooling of data but needs expansion to a prospective endocrine neoadjuvant trial to shift therapy from empiricism to an evidence-based modality.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Translational Cancer Research*. The article did not undergo external peer review.

Conflicts of Interest: The author has completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-592/coif). The author has no conflicts of interest to declare.

Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Ben Dhiab T, Bouzid T, Gamoudi A, et al. Male breast cancer: about 123 cases collected at the Institute Salah-Azaiz of Tunis from 1979 to 1999. Bull Cancer 2005;92:281-5.
2. Liu T, Tong Z, He L, Zhang L. Clinicopathological Characteristics and Survival Analysis of 87 Male Breast Cancer Cases. Breast Care (Basel) 2011;6:446-51.
3. Chen W, Wang H, Yang B, et al. Nomogram for predicting preoperative axillary lymph node status in male breast carcinoma: a SEER population-based study. Transl Cancer Res 2023;12:793-803.
4. Cutuli B, Le-Nir CC, Serin D, et al. Male breast cancer. Evolution of treatment and prognostic factors. Analysis of 489 cases. Crit Rev Oncol Hematol 2010;73:246-54.
5. Anderson WF, Althuis MD, Brinton LA, et al. Is male breast cancer similar or different than female breast cancer? Breast Cancer Res Treat 2004;83:77-86.
6. Cuzick J, Sestak I, Baum M, et al. Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 10-year analysis of the ATAC trial. Lancet Oncol 2010;11:1135-41.
7. Harlan LC, Zujewski JA, Goodman MT, et al. Breast cancer in men in the United States: a population-based study of diagnosis, treatment, and survival. Cancer 2010;116:3558-68.
8. Eggemann H, Altmann U, Costa SD, et al. Survival benefit of tamoxifen and aromatase inhibitor in male and female breast cancer. J Cancer Res Clin Oncol 2018;144:337-41.
9. Anelli TF, Anelli A, Tran KN, et al. Tamoxifen

administration is associated with a high rate of treatment-limiting symptoms in male breast cancer patients. Cancer 1994;74:74-7.
10. Visram H, Kanji F, Dent SF. Endocrine therapy for male breast cancer: rates of toxicity and adherence. Curr Oncol 2010;17:17-21.
11. Pemmaraju N, Munsell MF, Hortobagyi GN, et al. Retrospective review of male breast cancer patients: analysis of tamoxifen-related side-effects. Ann Oncol 2012;23:1471-4.
12. Xu S, Yang Y, Tao W, et al. Tamoxifen adherence and its relationship to mortality in 116 men with breast cancer. Breast Cancer Res Treat 2012;136:495-502.
13. Fontana D, Mari M, Martinelli A, et al. 3-month formulation of goserelin acetate ('Zoladex' 10.8-mg depot) in advanced prostate cancer: results from an Italian, open, multicenter trial. Urol Int 2003;70:316-20.
14. Abdel Azim H, Kassem L, Shohdy KS, et al. Durable Response of Androgen Receptor-Positive Male Breast Cancer to Goserelin. J Breast Cancer 2019;22:141-8.
15. Di Lauro L, Pizzuti L, Barba M, et al. Role of gonadotropin-releasing hormone analogues in metastatic male breast cancer: results from a pooled analysis. J Hematol Oncol 2015;8:53.

Cite this article as: Fentiman IS. Neoadjuvant treatment for male breast cancer. Transl Cancer Res 2023;12(7):1669-1671. doi: 10.21037/tcr-23-592

