Letter to the Editor

Postmastectomy radiation therapy in women with T1–T2 tumors and 1 to 3 positive lymph nodes: analysis of the breast international group 02-98 trial—a letter to the editor

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We would like to thank Gregucci *et al.* for their interest and analysis of our publication "Postmastectomy radiation therapy in women with T1–T2 tumors and 1 to 3 positive lymph nodes: analysis of the breast international group 02-98 trial" in which we highlighted the benefit of PMRT for patients with T1–T2 breast cancer and 1–3 positive LNs in the setting of modern chemotherapy.

This was an exhaustive retrospective analysis of a randomized clinical controlled trial investigating different systemic regimens including the addition of docetaxel to anthracycline based chemotherapy (1). Patients on that trial, and subsequently those in our analysis were treated with mastectomy and axillary nodal dissection. Our analysis of this patient population with primary tumors <5 cm and only 1–3 positive axillary lymph nodes highlighted the locoregional control benefit of adding RT in both the settings of anthracycline and anthracycline + docetaxel chemotherapy, albeit with a slightly lower benefit in patients treated with combination chemotherapy (5.7% *vs.* 3.3% absolute benefit respectively). This analysis did not reveal any significant breast cancer specific or overall survival advantages in the adjuvant RT group.

As highlighted by Gregucci *et al.* both the RT and no-RT groups were well balanced with the exception of higher number of 3 positive lymph nodes in the RT arm, which would have theoretically put this arm at a greater disadvantage. Despite this disadvantage, the addition of RT still added a locoregional benefit. It could even be hypothesized that this benefit would have been greater and may have even led to a mild survival advantage had the two groups been completely balanced.

Several classic trials in the "old" chemotherapy era showed a locoregional and survival advantage in adding adjuvant radiation. In fact, previous Danish and British Columbia randomized trials showed that the addition of radiation therapy had a 10-year absolute increase of locoregional control by over 20% and overall survival by around 10% (2-4). Even in the setting of 1–3 lymph nodes, the EBCTCG meta-analysis, which looked at individual data for 8,135 women in 22 trials, showed locoregional and survival benefit (5). While this data, might be outdated due to advances in systemic therapy and quality of surgical management, at least 2 contemporary studies, namely EORTC 22922 and NCIC MA. 20, show that in the setting of low lymphatic burden or node negative disease with high risk features, adding comprehensive nodal irradiation confers a small disease-free survival advantage when compared to breast/chest wall only radiation (6,7).

This information begs the question, if more radiated areas is better than less radiation, how much more so is comprehensive radiation better than no irradiation at all? Due to the above studies, the NCCN currently recommends giving adjuvant chest wall and comprehensive nodal irradiation to patients with 1-3 positive lymph nodes (8).

While it is true that our analysis couldn't account for the missing data on the tumor biologic parameters such as HER-2 status and luminal subtype, we acknowledge the limited role of these parameters in the omission of RT. The ASCO/ASTRO/SSO consensus guidelines clearly states that the decision to recommend PMRT or not requires a great deal of clinical judgement especially considering many factors including age of patients, tumor and axilla burden (1 *vs.* more than 1 lymph node), as well as size of the lymph nodes and tumor biology (9). Also, the St. Gallen consensus, while highlighting the importance of clinical judgement, does

not clearly recommend against adjuvant RT in the setting of N1 disease. Indeed, a majority agreed that regional nodal irradiation should be offered to N1 cancer patients with bad prognostic factors such as triple negative disease (10).

We agree with Gregucci *et al.* that our publication is limited by virtue of its retrospective nature, and thus drawing definitive conclusions needs to be cautioned. We eagerly await the results of upcoming randomized phase 3 trials such as MRC/EORTC SUPREMO, for more insight into the role of adjuvant radiation in this patient population (11). However, until such data is available to us, we do believe that the burden of evidence causes us to tailor decision on PMRT based on patients individual risks.

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Footnote

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Ethical Statement: The authors are 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.

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