Ann Surg Oncol (2024) 31:1669–1670
https://doi.org/10.1245/s10434-023-14563-4

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

LETTER – BREAST ONCOLOGY

Reply to: "Is Choosing Wisely Wise for Lobular Carcinoma in Patients Over 70 Years of Age? A National Cancer Database Analysis of Sentinel Node Practice Patterns

Nicole Goldhaber, MD, MA[1], Thomas O'Keefe, MD[1], and Sarah Blair, MD[2]

[1]Department of Surgery, University of California San Diego, San Diego, CA; [2]Moores Cancer Center, University of California San Diego, San Diego, CA

Dear Editor,

We would like to thank Mukhtar et al. for their queries,[1] and deeply appreciate their interest and the detailed insights provided regarding our recent article on sentinel lymph node biopsy practice patterns in women older than 70 years of age with T1 invasive lobular carcinoma (ILC) compared with those with invasive ductal carcinoma (IDC).[2]

First, the correspondent astutely brings forward the pivotal role of tumor biology, complemented by gene expression assays, in guiding breast cancer treatment decisions. Indeed, the availability of new systemic treatments has added new dimensions to the treatment decision matrix, in addition to shifts from axillary staging, as we demonstrate in our investigation.

The authors reference the phase III MonarcheE study that assessed the effect on outcomes of the addition of adjuvant abemaciclib to endocrine therapy for patients with hormone-positive, HER2-negative, node-positive early breast cancer. The authors comment that subgroup analysis in that study demonstrated treatment benefit even among patients aged 65 years and older. However, the effect on patients aged >65 years of age was insignificant for both invasive disease-free survival and distant relapse-free survival and was one of only five of the 30 subgroups tested that did not demonstrate a significant improvement in these outcomes.[3] This was not just due to the small sample size, as the estimated treatment effect was less for patients aged 65 years and older for both outcomes. While forest plots were not offered for overall survival, given the absence of a difference in the survival curves for the overall cohort coupled with the absence of a significant difference in invasive and distant relapse-free survival for patients aged >65 years, it is likely that the incorporation of adjuvant abemaciclib did not increase overall survival among patients older than 65 years of age. In fact, although the ages of the patients who died in the study were not offered in the manuscript or appendix, it is hypothetically possible that the reverse may be true, given that the most commonly reported grade 3–4 adverse events reported for patients whose regimen included abemaciclib are those that are disproportionately dangerous to geriatric patients, such as neutropenia (19.6 vs. 0.9%), leukopenia (11.4 vs. 0.4%), and diarrhea (7.8 vs. 0.2%). It is feasible that on a large scale, the addition of abemaciclib might negatively impact overall survival in patients older than 65 years of age. While the MonarchE study used a cut-off age of 65 years, we investigated patients aged 70 years and older, hence these concerns are arguably of greater clinical significance to our cohort. We would thus advise some caution regarding the application of the results of this study to the geriatric population.

The authors also insightfully point out that the higher discordance rate in clinical and pathologic staging for patients with ILC may limit the applicability of our results. To address this, we reperformed our analysis for patients with clinical T1 disease and found a nodal positivity rate of 10.5% for patients with ILC relative to 9.6% for IDC. This is in comparison with our initial results for patients with pathologic T1 disease of 8.2% for ILC compared with 8.8% for IDC—a difference between histologic subtypes of <1% in both cohorts, which we still feel is clinically insignificant.

First Received: 20 October 2023
Accepted: 24 October 2023
Published online: 28 November 2023

N. Goldhaber, MD, MA
e-mail: nhgoldhaber@health.ucsd.edu

The authors also asked an intriguing question regarding the number of positive nodes identified on sentinel lymph node biopsy. Among patients with clinical T1 ILC, we found a mean number of positive nodes of 1.38 compared with 1.22 for patients with IDC, a difference we feel again is not clinically significant.

We appreciate the queries of Mukhtar et al., but based on our reanalysis showing similarly low rates of nodal positivity in this population, surgeons can continue to Choose Wisely in women over 70 years of age with early-staged lesions for both IDC and ILC.

Warm regards,

Nicole H. Goldhaber, Thomas O'Keefe, Sarah Blair

DISCLOSURE Thomas O'Keefe started a fellowship in breast surgery at the University of California San Diego in August 2024 and Rita Mukhtar is one of his surgical attendings. Both Thomas O'Keefe and Rita Mukhtar have collaborated in the past on a different project, however they have discussed neither the manuscript under discussion nor the letter to the editor written by Rita Mukhtar. This information in no way influenced Thomas O'Keefe's participation in the drafting of a response.

REFERENCES

1. Muktar RA, Huppert L, Ramalingam K. Letter to the Editor of Annals of Surgical Oncology concerning "Is Choosing Wisely Wise for lobular carcinoma in patients over 70 years of age? A National Cancer Database analysis of sentinel node practice patterns". *Ann Surg Oncol.* 2023. https://doi.org/10.1245/s10434-023-14474-4.
2. Goldhaber NH, O'Keefe T, Kang J, Douglas S, Blair SL. Is Choosing Wisely wise for lobular carcinoma in patients over 70 years of age? A National Cancer Database analysis of sentinel node practice patterns. *Ann Surg Oncol*. 2023;30(10):6024–32.
3. Johnston SRD, Toi M, O'Shaughnessy J, et al. Abemaciclib plus endocrine therapy for hormone receptor-positive, HER2-negative, node-positive, high-risk early breast cancer (monarchE): results from a preplanned interim analysis of a randomised, open-label, phase 3 trial. *Lancet Oncol*. 2023;24(1):77–90. https://doi.org/10.1016/S1470-2045(22)00694-5.