



Published in final edited form as:

*JAMA Surg.* 2023 October 01; 158(10): 1021–1022. doi:10.1001/jamasurg.2023.2856.

## Will Targeted Axillary Surgery Suffice for Adjuvant Treatment Decision-Making?

Margaret S. Pichardo, MD, PhD, MPH,

Jennifer Q. Zhang, MD,

Oluwadamilola M. Fayanju, MD, MA, MPHS

Department of Surgery, Hospital of the University of Pennsylvania, Philadelphia (Pichardo); Division of Breast Surgery, Department of Surgery, Perelman School of Medicine, The University of Pennsylvania, Philadelphia (Zhang, Fayanju); Rena Rowan Breast Center, Abramson Cancer Center, Penn Medicine, Philadelphia, Pennsylvania (Zhang, Fayanju); Penn Center for Cancer Care Innovation, The University of Pennsylvania, Philadelphia (Fayanju); Leonard Davis Institute of Health Economics, The University of Pennsylvania, Philadelphia (Fayanju).

Weber and colleagues<sup>1</sup> have published the results of a preplanned prospective observational cohort study of the first 500 randomized patients in the international, multicenter, phase3 Tailored Axillary Surgery With or Without Axillary Lymph Node Dissection Followed by Radiotherapy in Patients With Clinically Node-Positive Breast Cancer (TAXIS) trial. This substudy was designed to address the association of staging information gleaned from axillary lymph node dissection (ALND) with adjuvant systemic therapy treatment decisions in 2 groups of patients with breast cancer: (1) patients with clinically node (cN)-positive breast cancer who undergo upfront surgery and (2) patients with cN-positive breast cancer and persistent nodal disease after neoadjuvant chemotherapy (NACT). For this study, the analytic cohort consisted of patients who underwent targeted axillary surgery (TAS), defined as removal of sentinel and palpable lymph nodes, from August 2018 through June 2022. The authors found that although omission of ALND in the patients who only received TAS plus axillary radiotherapy led to understaging of patients with cN-positive disease and significant axillary tumor burden, not knowing the exact number of positive nodes was not significantly associated with adjuvant treatment decisions in either recipients of NACT or upfront surgery, even if involved lymph nodes were, by implication, left behind.

This study is limited by its observational design, absence of a prespecified power analysis to optimize sample size, and low numbers of patients with hormone receptor (HR)-negative/*ERBB2* (formerly *HER2* or *HER2/neu*)-positive disease. This study also did not require a standardized approach to TAS: neither dual tracer nor localization of the clipped node was required, and type of tracer was not specified, limiting quality control assessments. Although we recognize this flexibility may enable generalizability of study findings to clinical settings in which axillary localization is not possible, these limitations raise questions as

**Corresponding Author:** Oluwadamilola M. Fayanju, MD, MA, MPHS, Division of Breast Surgery, Department of Surgery, Perelman School of Medicine, University of Pennsylvania, 3400 Spruce St, Silverstein 4, Philadelphia, PA 19104 (fayanju@upenn.edu).

**Disclaimer:** The content of this manuscript is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

to the reproducibility of TAS as an alternative to ALND and its concomitant outcomes across different surgeons, institutions, and countries. Also not addressed is whether TAS is noninferior to targeted axillary dissection (TAD, which includes sentinel lymph node biopsy and localized excision of the clipped node)<sup>2</sup> in disease staging and whether differences between these 2 more limited forms of axillary surgery may have implications for treatment selection and (to be assessed via the larger TAXIS trial) oncologic outcomes. Finally, additional studies will be needed to clarify whether limiting axillary surgery will affect systemic therapy decisions for cyclin-dependent kinase (CDK) 4/6 inhibitors in HR-positive breast cancer. The study by Weber and colleagues<sup>1</sup> does provide reassurance that ALND should not be performed solely for the purpose of facilitating adjuvant therapy decision-making, but additional prospective findings from TAXIS<sup>3</sup> and other trials<sup>4</sup> will be needed to elucidate optimal approaches to limited axillary surgery and what the longterm oncologic implications of surgical de-escalation in the axilla will be.

### Conflict of Interest Disclosures:

Dr Fayanju reported receiving grants from the National Institutes of Health, having a collaborative research agreement with Gilead Sciences Inc, and receiving consultant fees from Sanofi outside the submitted work. No other disclosures were reported.

### REFERENCES

1. Weber WP, Matrai Z, Hayoz S, et al. ; TAXIS Study Writing Group. Association of axillary dissection with systemic therapy in patients with clinically node-positive breast cancer. *JAMA Surg*. Published online July 19, 2023. doi:10.1001/jamasurg.2023.2840
2. Caudle AS, Yang WT, Krishnamurthy S, et al. Improved axillary evaluation following neoadjuvant therapy for patients with node-positive breast cancer using selective evaluation of clipped nodes: implementation of targeted axillary dissection. *J Clin Oncol*. 2016;34(10):1072–1078. doi:10.1200/JCO.2015.64.0094 [PubMed: 26811528]
3. Henke G, Knauer M, Ribi K, et al. Tailored axillary surgery with or without axillary lymph node dissection followed by radiotherapy in patients with clinically node-positive breast cancer (TAXIS): study protocol for a multicenter, randomized, phase 3 trial. *Trials*. 2018;19(1):667. doi:10.1186/s13063-018-3021-9 [PubMed: 30514362]
4. Kuemmel S, Heil J, Rueland A, et al. A prospective, multicenter registry study to evaluate the clinical feasibility of targeted axillary dissection (TAD) in node-positive breast cancer patients. *Ann Surg*. 2022;276(5):e553–e562. doi:10.1097/SLA.0000000000004572 [PubMed: 33156057]