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LETTER TO THE EDITOR

Node Micrometastases Detection After Neoadjuvant Chemotherapy in Breast Cancer: Is It of Clinical Value?

TO THE EDITORS:

It is thought that detection of micrometastases (mi) or isolated tumor cells (ITCs) in sentinel lymph node biopsy (SLNB) or axillary lymph nodes (ALNs) in breast cancer can have prognostic and predictive clinical utility. The American Joint Committee on Cancer (AJCC) recommends lymph node classification into: pN0 (no metastases > 2 mm), pN1mi (small metastases > 0.2 mm to < 2 mm) and pN0(i +) (ITC deposits < 0.2 mm). However, nobody knows whether detection of mi or ITCs in SNLB should be followed by axillary lymph node dissection (ALND) or if this identification of minimal disease in SLNB or ALNs is a predictive marker for response to adjuvant chemotherapy offering a survival benefit. Even more complicated is the topic of detection of mi or ITCs in ALNs after neoadjuvant chemotherapy (NAC). However, even if mi or ITCs detection has prognostic value, what is the clinical utility given that NAC has been completed?

Sakakibara and colleagues aim to approach these still unanswered questions.[1] In their report published in the September issue of the *Annals of Surgical Oncology*, they retrospectively analyzed the data of 80 patients with a diagnosis of cytologically proven axillary metastases who received NAC. Using multislice sectioning and cytokeratin immunohistochemistry, all patients were categorized into four groups: no metastasis with conventional or microscopic examination, pN0(i +), pN1mi, and pN1 (metastases > 2 mm). Survival was significantly better among patients with no nodal metastasis or ITCs in lymph nodes than in those with nodal micrometastases. The authors conclude that residual micrometastatic (pN1mi) disease but not presence of ITCs in ALNs after NAC for patients with cytologically proven axillary metastases on initial diagnosis is a predictor of poor survival.

Although this is not an unexpected finding, the study is limited by the lack of randomization and the very small number of patients in each of the four subgroups evaluated. However, even if large randomized trials prove the prognostic importance of residual micrometastases in axillary lymph nodes after completion of neoadjuvant therapy, the clinical implication will remain limited.

Current and future research efforts are focused on the development of molecular markers to predict prognosis and response to specific therapies. The use of micrometastases or ITCs in sentinel and nonsentinel axillary lymph nodes as well as of multigene assays including the 21-gene assay (Oncotype DX) and the 70-gene signature (Mammaprint) have provided promising results.[2] On the basis of these positive findings all these potential markers are undergoing prospective evaluation in large phase III randomized controlled trials. Until then, however, decision-making considering all these tools should be very careful analyzed and take into account multiple clinicopathologic and treatment variables.[2–4]

Predicting oncological outcome and response under various neoadjuvant chemotherapeutic regimens before treatment initiation is a major challenge. However, new technologies facilitate genetics and genomics applications, allowing optimism.[5–9]

Dimosthenis Ziogas, MD, Haralampos Harissis, MD, and Charalabos Batsis, MD
Department of Surgery, School of Medicine, University of Ioannina, Ioannina, Greece
e-mail: deziogas@hotmail.com

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REFERENCES

1. Sakakibara M, Nagashima T, Kadowaki M, et al. Clinical significance of axillary microresiduals after neoadjuvant chemotherapy in breast cancer patients with cytologically proven metastases. *Ann Surg Oncol*. 2009;16(9):2470–8.
2. Roukos DH. Twenty-one-gene assay: challenges and promises in translating personal genomics and whole-genome scans into personalized treatment of breast cancer. *J Clin Oncol*. 2009;27(8):1337–8.
3. Ziogas D, Roukos DH. Genetics and personal genomics for personalized breast cancer surgery: progress and challenges in

research and clinical practice. *Ann Surg Oncol*. 2009;16(7):1771–82.
4. Roukos DH. Radiation therapy for breast cancer. *N Engl J Med*. 2009;360(13):1362–3.
5. Roukos DH. Breast cancer outcomes: the crucial role of the breast surgeon in the era of personal genetics and systems biology. *Ann Surg*. 2009;249(6):1067–8.
6. Roukos DH. Personalized cancer diagnostics and therapeutics. *Expert Rev Mol Diagn*. 2009;9(3):227–9.
7. Roukos DH. Mea Culpa with cancer-targeted therapy: new thinking and new agents design for novel, causal networks-based, personalized biomedicine. *Expert Rev Mol Diagn*. 2009;9(3): 217–21.
8. Ziogas D, Roukos DH. CDH1 testing: can it predict the prophylactic or therapeutic nature of total gastrectomy in hereditary diffuse gastric cancer? *Ann Surg Oncol*. 2009;16(10):2678–81.
9. Roukos DH. Genome-wide association studies: how predictable is a person's cancer risk? *Expert Rev Anticancer Ther*. 2009;9(4): 389–92.