JOURNAL OF CLINICAL ONCOLOGY CORRESPONDENCE

Prognosis of T1ab Node-Negative Human Epidermal Growth Factor 2–Positive Breast Carcinomas

TO THE EDITOR: We have read with great interest the article by Fehrenbacher et al about prognosis of T1abN0 human epidermal growth factor 2 (HER2) –positive breast carcinomas.[1] The authors should be congratulated for their significant contribution to this topic with a large cohort of well-followed patients; nonetheless, we would like to discuss their conclusions. Indeed, the authors conclude that patients with T1ab tumors ≤ 9 mm have a good prognosis with a low risk of distant recurrence, whereas those with 10-mm tumors have a higher risk. On the basis of these data, the authors strongly suggest that patients with T1abN0 HER2-positive tumors of less than 10 mm should not receive adjuvant trastuzumab (Hoffmann-La Roche, Basel, Switzerland) -based chemotherapy (ATBC).

In our opinion, three main pitfalls may be observed in their data interpretation.[1] First, 20 of the 116 patients in the T1a group had in fact a T1mi tumor (invasive tumor size ≤ 0.1 cm). Because unifocal T1miN0 breast carcinomas have a negligible risk of distant recurrence, the distant-recurrence–free interval (DRFI) is probably overestimated in their T1a group. Actually, adjuvant chemotherapy is not discussed in T1miN0 carcinomas in current guidelines.[2] Second, Fehrenbacher et al[1] explored only two prognosis factors: size and estrogen receptor status. Other prognosis factors such as lymphovascular invasion, tumor grade, or mitotic index should have been evaluated in an adjusted analysis. Third, a significant proportion of patients received adjuvant chemotherapy, trastuzumab, or both (17% of T1a cases excluding T1mi, and 40% of T1b cases). By including this treated population in their Kaplan-Meier estimates of DRFI, Fehrenbacher et al presumed a priori that adjuvant chemotherapy and trastuzumab were not effective in preventing distant recurrences. Once again, the DRFI might be overestimated for both T1a and T1b cases.

We have published a large retrospective series of T1abN0 HER2-positive cases with 129 patients treated with ATBC and 123 treated with neither chemotherapy nor trastuzumab.[3,4] Factors retrospectively associated with ATBC prescription were size > 5 mm, estrogen receptor negativity, high Elston-Ellis grade, younger age, and, above all, date of diagnosis after the American Society of Clinical Oncology 2005 Annual Meeting. To compensate for selection bias (patients with higher risk being the ones treated with ATBC), we used a propensity score for adjusted survival analysis.[5] In our analysis, size was not independently associated with prognosis. We then observed in our series a significant 40-month disease-free survival benefit for patients treated with ATBC, mostly in cases without hormone receptor expression and/or with lymphovascular invasion. Of note, several other studies have found similar results.[6-10]

The favorable prognosis of T1abN0 HER2-positive tumors observed in the article by Fehrenbacher et al may merely be due to the integration of T1mi cases and to the use of adjuvant chemotherapy and/or trastuzumab in 27% of patients. We think that size may not be the most important prognosis factor in T1abN0 HER2-positive breast carcinomas and that other prognosis factors should be considered. In our opinion, ATBC should be considered whatever the tumor size in T1abN0 HER2-positive cases with lymphovascular invasion or in case of hormone receptor negativity.

Luc Cabel
Institut Curie, Paris, France

Julien Péron
Centre Hospitalier de Lyon-Sud, Lyon, France

Paul Henri Cottu and Manuel Jorge Rodrigues
Institut Curie, Paris, France

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at www.jco.org.

REFERENCES

1. Fehrenbacher L, Capra AM, Quesenberry CP Jr, et al: Distant invasive breast cancer recurrence risk in human epidermal growth factor receptor 2–positive T1a and T1b node-negative localized breast cancer diagnosed from 2000 to 2006: A cohort from an integrated health care delivery system. J Clin Oncol 32:2151-2158, 2014
2. National Comprehensive Cancer Network Guidelines: Breast cancer version 3.2014. http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf
3. Rodrigues MJ, Péron J, Frénel J-S, et al: Benefit of adjuvant trastuzumab-based chemotherapy in T1ab node-negative HER2-overexpressing breast carcinomas: A multicenter retrospective series. Ann Oncol 24:916-924, 2013
4. Rodrigues MJ, Wassermann J, Albiges L, et al: Trastuzumab treatment in t1ab, node-negative, human epidermal growth factor receptor 2-overexpressing breast carcinomas. J Clin Oncol 28:e541-542, 2010
5. Groenwold RH, Hak E, Hoes AW: Quantitative assessment of unobserved confounding is mandatory in nonrandomized intervention studies. J Clin Epidemiol 62:22-28, 2009
6. McArthur HL, Mahoney KM, Morris PG, et al: Adjuvant trastuzumab with chemotherapy is effective in women with small, node-negative, HER2-positive breast cancer. Cancer 117:5461-5468, 2011
7. Horio A, Fujita T, Hayashi H, et al: High recurrence risk and use of adjuvant trastuzumab in patients with small, HER2-positive, node-negative breast cancers. Int J Clin Oncol 17:131-136, 2012
8. Migdady Y, Sakr BJ, Sikov WM, et al: Adjuvant chemotherapy in T1a/bN0 HER2-positive or triple-negative breast cancers: Application and outcomes. Breast 22:793-798, 2013
9. Seal MD, Speers CH, O'Reilly S, et al: Outcomes of women with early-stage breast cancer receiving adjuvant trastuzumab. Curr Oncol 19:197-201, 2012
10. Webster RM, Abraham J, Palaniappan N, et al: Exploring the use and impact of adjuvant trastuzumab for HER2-positive breast cancer patients in a large UK cancer network. Do the results of international clinical trials translate into a similar benefit for patients in South East Wales? Br J Cancer 106:32-38, 2012

DOI: 10.1200/JCO.2014.58.6941; published online ahead of print at www.jco.org on December 15, 2014

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Prognosis of T1ab Node-Negative Human Epidermal Growth Factor 2–Positive Breast Carcinomas

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or jco.ascopubs.org/site/ifc.

Luc Cabel
No relationship to disclose

Julien Péron
Travel, Accommodations, Expenses: Hoffmann-La Roche

Paul Henri Cottu
No relationship to disclose

Manuel Jorge Rodrigues
Research Funding: Novartis
Travel, Accommodations, Expenses: Hoffmann-La Roche, Novartis, Chugai Pharma
Other Relationship: Chugai Pharma