

## Letter to the Editor



# Adjuvant Trastuzumab Is Required in Human Epidermal Growth Factor Receptor 2-Positive Node-Negative Breast Cancer Patients Regardless of Tumour Size

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### Conflict of Interest

The authors declare that they have no competing interests.

### Author Contributions

Conceptualization: Bender L, Pivot X; Formal analysis: Bender L, Pivot X; Methodology: Bender L, Pivot X; Software: Pivot X; Supervision: Pivot X; Validation: Kurtz JE, Petit T, Pivot X; Visualization: Pivot X; Writing - original draft: Bender L, Pivot X.

The survival benefit of adjuvant trastuzumab plus chemotherapy in early-stage breast cancer has been established by the results of 3 large randomized studies [1-3]. These historical trials included early-stage breast cancer with a tumour size larger than 10 millimetres to warrant enough materials for central review of human epidermal growth factor receptor 2 (HER2) status assessment. The inclusion criteria from these studies laid the foundation for the current indications for routine use of trastuzumab. The question considering the benefit of adjuvant trastuzumab in pT1N0 HER2 positive breast cancer is still debated [4-7]. We retrospectively reported patients with small HER2-positive breast cancers without nodal involvement at the University Hospital of Strasbourg (France) between January 2004 and December 2009. Such clinical characteristics are considered borderline indications for adjuvant trastuzumab, as based on the initial inclusion criteria used in previous historical trials. This present retrospective study did not consider the reasons for the given treatments and only analysed the impact, if any, of trastuzumab on survival outcomes. A cohort of 55 patients with borderline characteristics for adjuvant trastuzumab eligibility was identified in the hospital database. Thirty-five (64%) tumours had positive tumoural hormone-receptor expression, and all cases were free of nodal axillary involvement. Tumour size ranged from 1 to 5 mm, 6 to 10 mm and 11 to 15 mm in 12 (24%), 21 (38%) and 22 (38%) cases, respectively. Among the 55 patients, 36 (65%) were treated by an adjuvant trastuzumab-containing regimen (5 trastuzumab only; 31 trastuzumab plus chemotherapy); on the other hand, 19 (34%) patients had no adjuvant treatment (n=7) or received endocrine therapy alone (n=12). In the group treated with adjuvant trastuzumab, no recurrence was observed, while 2 recurrences (10.5%; 95% confidence interval=7.34-13.66) were reported in the group not receiving trastuzumab. Trastuzumab was related to one occurrence of asymptomatic decrease in left ventricular function (New York Heart Association stage I), which fully recovered following treatment interruption. In small tumours (T1a and T1b, without nodal involvement), the risk may be underestimated; for example, the risk of recurrence was not 0% and ranged up to 10% in our cohort. Because no recurrence was reported in the group treated with trastuzumab, one might consider exposure to adjuvant trastuzumab in all HER2-positive breast cancers. A large study reported by van Ramshorst et al. [8] concluded similar results. Indeed, in this cohort including 3,512 patients with pT1a/b/c HER2-positive tumours, trastuzumab improved survival and should be given to all patients with small node-negative HER2-positive breast cancer. In view of these results, we support the statement that all patients with HER2-positive breast cancer, regardless of tumour size, should receive adjuvant trastuzumab.

## REFERENCES

1. Piccart-Gebhart MJ, Procter M, Leyland-Jones B, Goldhirsch A, Untch M, Smith I, et al. Trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer. *N Engl J Med* 2005;353:1659-72.  
[PUBMED](#) | [CROSSREF](#)
2. Slamon D, Eiermann W, Robert N, Pienkowski T, Martin M, Press M, et al. Adjuvant trastuzumab in HER2-positive breast cancer. *N Engl J Med* 2011;365:1273-83.  
[PUBMED](#) | [CROSSREF](#)
3. Romond EH, Perez EA, Bryant J, Suman VJ, Geyer CE Jr, Davidson NE, et al. Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. *N Engl J Med* 2005;353:1673-84.  
[PUBMED](#) | [CROSSREF](#)
4. Curigliano G, Viale G, Bagnardi V, Fumagalli L, Locatelli M, Rotmensz N, et al. Clinical relevance of *HER2* overexpression/amplification in patients with small tumor size and node-negative breast cancer. *J Clin Oncol* 2009;27:5693-9.  
[PUBMED](#) | [CROSSREF](#)
5. He X, Ji J, Tian M, Esteva FJ, Hortobagyi GN, Yeung SJ. Long-term survival analysis of adjuvant chemotherapy with or without trastuzumab in patients with T1, node-negative HER2-positive breast cancer. *Clin Cancer Res* 2019;25:7388-95.  
[PUBMED](#) | [CROSSREF](#)
6. Kubo M, Kawai M, Kumamaru H, Miyata H, Tamura K, Yoshida M, et al. A population-based recurrence risk management study of patients with pT1 node-negative HER2+ breast cancer: a National Clinical Database study. *Breast Cancer Res Treat* 2019;178:647-56.  
[PUBMED](#) | [CROSSREF](#)
7. de Nonneville A, Gonçalves A, Zemmour C, Classe JM, Cohen M, Lambaudie E, et al. Benefit of adjuvant chemotherapy with or without trastuzumab in pT1ab node-negative human epidermal growth factor receptor 2-positive breast carcinomas: results of a national multi-institutional study. *Breast Cancer Res Treat* 2017;162:307-16.  
[PUBMED](#) | [CROSSREF](#)
8. van Ramshorst MS, van der Heiden-van der Loo M, Dackus GM, Linn SC, Sonke GS. The effect of trastuzumab-based chemotherapy in small node-negative HER2-positive breast cancer. *Breast Cancer Res Treat* 2016;158:361-71.  
[PUBMED](#) | [CROSSREF](#)