Trastuzumab and Chemotherapy May Be Appropriate for Small, Node-Negative, HER2-Positive Breast Cancer

PATRICK G. MORRIS,^a HEATHER L. MCARTHUR

Breast Cancer Medicine Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, New York, USA

Disclosures: Heather L. McArthur: GlaxoSmithKline, Bristol-Myers Squibb, Genentech, Roche (H). The other author indicated no financial relationships.

(C/A) Consulting/advisory relationship; (RF) Research funding; (E) Employment; (H) Honoraria received; (OI) Ownership interests; (IP) Intellectual property rights/inventor/patent holder; (SAB) Scientific advisory board

This challenging case presented by Drs. Connolly and Bardia represents a relatively common scenario in breast medical oncology clinics [1]. The fundamental challenge is one of risk-benefit stratification. As cited by the contributors, recently reported data from MD Anderson and British Columbia indicates that women with small, node-negative, HER2-positive tumors are at a higher risk of distant recurrence than was previously appreciated. Yet, the absolute benefits of systemic therapy for these patients has been uncertain, as these lower risk populations were not included in the large randomized adjuvant trastuzumab studies. As pointed out by Drs. Connolly and Bardia, the evidence in support of the use of adjuvant chemotherapy and trastuzumab is based largely on retrospective studies and subset analyses from randomized trials.

At Memorial Sloan-Kettering Cancer Center, we recently reported a retrospective, sequential cohort study of women with T1, N0, HER2-positive breast cancer [2]. Patient outcomes were compared between 106 trastuzumab-untreated women who were diagnosed before the first report of the benefits of adjuvant trastuzumab in 2005 and 155 trastuzumab-treated women who were diagnosed after 2005. The 3-year distant recurrence-free survival was 95% for patients in the trastuzumab cohort versus 100% for patients who did not receive trastuzumab ($p = .0072$). Importantly, all women in the trastuzumab cohort received adjuvant chemotherapy versus 66% of the patients who did not receive trastuzumab. There-

fore, this study does not provide information as to how much of the observed benefit can be ascribed specifically to trastuzumab versus chemotherapy administration.

Interestingly, the trastuzumab-treated cohort may have been at slightly higher risk of recurrence overall (based on slightly larger tumor size and higher proportion of women with lymphovascular invasion). When combined with the observed reduction in the event rate in this cohort, the hypothesis that such patients benefit from trastuzumab chemotherapy is strengthened. In addition, we performed a subset analysis of women with tumors ≤ 1.0 cm in size and saw consistent benefits: Distant recurrence-free survival was 97% (95% confidence interval: 92%–100%) versus 100% ($p = .2985$) in favor of chemotherapy/trastuzumab-treated cohort.

These findings are consistent with the National Comprehensive Cancer Network recommendations for consideration of chemotherapy with or without trastuzumab for women with lymph node-negative tumors that are 0.6–1 cm in size [3]. Clearly, the decision to prescribe postoperative chemotherapy and trastuzumab should be individualized based on careful consideration of the risks and benefits.

AUTHOR CONTRIBUTIONS

Conception/Design: Patrick G. Morris, Heather McArthur

Collection and/or assembly of data: Patrick G. Morris, Heather McArthur

Manuscript writing: Patrick G. Morris, Heather McArthur

Final approval of manuscript: Patrick G. Morris, Heather McArthur

REFERENCES

1. Connolly RM, Bardia A. Trastuzumab for small HER2+ breast cancer: Small tumor, big decision. *The Oncologist* 2012;17:508–511.

2. 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* 2011;117:5461–5468.

3. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Breast Cancer, Version 1.2012. Available at http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed June 20, 2012.

Correspondence: Patrick G. Morris, M.D., Breast Cancer Medicine Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10065, USA. Telephone: 001-646-888-4551; Fax: 001-646-888-4555; e-mail: morrisp1@mskcc.org Received July 25, 2012; accepted for publication August 17, 2012. ©AlphaMed Press 1083-7159/2012/\$20.00/0 <http://dx.doi.org/10.1634/theoncologist.2012-0318>