Trastuzumab Combined with Paclitaxel after Doxorubicin and Cyclophosphamide for Operable HER2-Positive Breast Cancer

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Concerning the controversies in the use of trastuzumab for early-stage breast cancer, Cianfrocca and Gradishar [1] have recently reported that an unplanned interim analysis of the North Central Cancer Treatment Group N9831 trial revealed a 36% relative reduction in the risk for recurrence for concurrent compared with sequential trastuzumab ($p = .0114$) [2], even though further follow-up is needed to ascertain whether this trend continues.

Romond et al. [3] have recently presented the combined results of two trials that compared adjuvant chemotherapy with or without concurrent trastuzumab in women with surgically removed HER2-positive breast cancer. The authors conclude that trastuzumab combined with paclitaxel after doxorubicin and cyclophosphamide improves outcomes among women with surgically removed HER2-positive breast cancer. In trial B-31, 805 patients received doxorubicin and cyclophosphamide every 21 days for four cycles followed by paclitaxel every 3 weeks for four cycles plus weekly trastuzumab for 52 weeks; in only 59 patients, paclitaxel was given weekly for 12 weeks. In trial N9831, 808 patients were administered doxorubicin and cyclophosphamide as in trial B-31 but followed by 12 weekly doses of paclitaxel plus weekly trastuzumab for 52 weeks.

It might be highlighted that exposure to lower and more frequent doses of paclitaxel could potentially exploit antiangiogenic and proapoptotic effects [4]. In metastatic breast cancer, weekly administration of paclitaxel has been reported to be superior to once-every-3-weeks administration, improved the likelihood of pathologic complete remission [6]. By contrast, Romond et al. [3] assert that there was no evidence that the benefit of trastuzumab differed significantly between the B-31 and N9831 trials. The finding that the same effect of trastuzumab was observed in both the studies deserves further investigation, given the difference in the paclitaxel schedule.

DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST
The authors indicate no potential conflicts of interest.

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IN REPLY

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Dr. Ferretti et al. [1] raise an interesting point in their letter commenting on our recent article, specifically regarding the potential benefit of paclitaxel administered weekly rather than every 3 weeks. As Dr. Ferretti points out, it has long been hypothesized that administering paclitaxel in a weekly fashion could lead to greater antiangiogenic and proapoptotic effects. When examined in randomized phase II and III trials, however, this hypothesis has not been fully validated. In the metastatic setting, for example, weekly paclitaxel was superior to every-3-weeks dosing in terms of response rate and time to progression but not overall survival [2]. More recently, the Eastern Cooperative Oncology Group 1199 trial, which compared docetaxel with paclitaxel and weekly with every-3-weeks dosing in 4,988 patients with early-stage breast cancer, did not show a statistically significant benefit for weekly taxane therapy [3]. Given these results, it is unlikely that a difference in benefit will be detected between the B-31 and N9831 trials based on taxane schedule.

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REFERENCES


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