

## Local Therapy in Stage IV Breast Cancer Patients

To the Editor:

With interest I read the retrospective analysis by Fields et al.<sup>1</sup> about breast surgery in stage IV breast cancer and the comment by Khan.<sup>2</sup> In this comment Khan clearly focuses on the main issues, namely how to use the retrospective data to design a prospective trial.

Regarding surgery, Khan et al. demonstrated<sup>3</sup> that local therapy has to include all standard procedures used in nonmetastasized patients such as axillary surgery and radiotherapy. In respect to stratification criteria, available data show that the number of metastasized organs (visceral versus nonvisceral) and the chemotherapeutic agent rather than comorbidity variants should be taken into consideration.<sup>1</sup>

I would like to highlight again the issue of timing the surgical procedure. The timing in such a prospective trial should depend on the possible underlying rationale why resection of the primary breast cancer should improve overall survival. To date the only plausible explanation is the self-seeding phenomenon<sup>4</sup> with cancer stem cells from the primary breast cancer that acts as a “mother ship.” In this regard, the only correct timing would be surgery right away. However, metastases are also able to produce cancer stem cells, thus making the resection of the primary cancer unnecessary.<sup>5</sup> In this regard, the biological rationale is still lacking and I cannot find more insight from physicians in their discussion. The fact that local therapy increases overall survival, however, is undisputed.<sup>6</sup>

It will be of interest for the readers that two prospective trials have already been initiated. The first in India started in February 2005 (NCT00193778), and the second in Turkey started in November 2007 (NCT00557986). The

India trial at Tata Memorial Hospital randomizes therapy responding patients after six cycles into two groups, surgery versus no surgery. The Turkey trial randomizes right away before any systemic therapy. We hope that similar trials will be under way in Europe and the United States.

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