In Reply

We appreciate the citation and comments in the letter by Fink et al. [1] regarding our recently published article in ***The Oncologist*** [2]. In response to this thoughtful letter, we would like to address the following points.

Although a study by Pierga et al. (not a randomized study) suggested similar disease-free survival (DFS) between groups that have or have not received adjuvant therapy [3], most randomized phase III studies demonstrated that, compared with surgery only, postsurgical adjuvant therapy significantly improved DFS and overall survival rates [4]. Bonadonna et al. reported a significant survival benefit for cyclophosphamide, methotrexate, and fluorouracil as adjuvant therapy over surgery only after 30 years of follow-up [5, 6].

It is believed that early recurrence within 1 year after completion of adjuvant therapy would exclude the possibility of reusing the same agents in the first-line metastatic setting. The patient, for example, is considered primarily resistant to docetaxel if the recurrence occurred within 1 year after completing docetaxel-based adjuvant therapy. Therefore, agents other than docetaxel should be considered. Nonetheless, how long the recurrence-free interval should be used as the cutoff point for indicating resistance remains controversial.

As stated by the authors of the letter, patients receiving adjuvant therapy are usually associated with worse prognosis, such as those at later stages, with higher tumor burden, or with aggressive subtypes. These intrinsic features, in fact, predetermined the different treatment outcomes.

Prior adjuvant therapy may lead to resistance, but it does not always do so. In practice, a comprehensive assessment incorporating the pathological and biological nature of the primary tumor, recurrence-free survival, previous treatment outcome, and other factors would be warranted to evaluate resistance and to determine an appropriate treatment plan.

Many factors contribute to patient survival in metastatic breast cancer and other late-stage cancers. They include but are not limited to patient performance status, organ functions, prior adjuvant therapy, and first-line and subsequent lines of therapy in the metastatic setting. It is doubtful that adjuvant therapy causes a worse survival outcome. This being said, should resistance develop following adjuvant therapy, the patient needs to be offered a first-line solution that is free of cross-resistance.

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