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LETTER TO THE EDITOR

Does the sequence of taxane administration affect the outcome of patients with breast cancer in the adjuvant and neoadjuvant settings?

Ali Alkan · Ugur Sahin · Kadri Altundag

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To The Editor,

Taxane- and anthracycline-containing chemotherapy regimens are commonly used for the treatment of breast cancer both in the adjuvant and in the neoadjuvant settings. Recently, there has been a concern about the sequencing of these two drugs. In a recent randomized phase III study by the Hellenic Oncology Research Group, three weekly docetaxel followed by epirubicin/cyclophosphamide (E/C) combination was compared with epirubicin/cyclophosphamide/5-fluorouracil (FEC) regimen as adjuvant chemotherapy in women with axillary node-positive early breast cancer (1). Five-year disease-free survival was found to be better in the sequential docetaxel followed by E/C group (72.6 vs. 67.2%, $P = 0.041$). Furthermore, the first report of the Neo-tAnGo study, a neoadjuvant randomized phase III trial of E/C and paclitaxel ± gemcitabin in high risk early breast cancer has also concluded that the sequence of taxane first regimen had a significant advantage in pathological complete response rate than sequence of anthracycline first regimen (20 vs. 15%, $P = 0.03$) (2).

Some proposals were put forward for the mechanism of this sequencing. A study by Taghian et al. (3) evaluated the interstitial fluid pressure (IFP) and oxygenation before and after neoadjuvant chemotherapy with weekly paclitaxel and doxorubicin in breast cancer patients with a tumor size of ≥3 cm. Paclitaxel was found to significantly increase IFP and oxygenation, whereas doxorubicin not. Thus, paclitaxel may exhibit positive effects by altering the IFP barrier, which may restrict the tumor cells to enter the circulation. It may also increase the anthracycline drug concentration at tumor tissue level if taxane is given before the anthracyline administration.

In conclusion, we propose that taxane followed by anthracycline administration may be a more optimal regimen than anthracycline first followed by taxane schedule for both neoadjuvant and adjuvant treatment of breast cancer patients. Further studies are needed to confirm this proposal.

A. Alkan · U. Sahin
Department of Internal Medicine, Hacettepe University School of Medicine, Ankara, Turkey

K. Altundag (✉)
Department of Medical Oncology, Hacettepe University Institute of Oncology, 06100 Sihhiye, Ankara, Turkey
e-mail: altundag66@yahoo.com

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