Optimal choice of adjuvant chemotherapy regimen for EBC

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The most effective chemotherapeutic agent in the treatment of breast cancer has been anthracyclines since the 1980's. The taxanes were integrated into breast cancer management as being equally or even more effective than the anthracyclines since the 1990's, and with the advance of new cytotoxic (capecitabine, gemcitabine, vinorelbine) or targeted biological agents (trastuzumab, lapatinib, bevacizumab) since this century, the landscape of systemic breast cancer treatment is undergoing revolutionary changes. Anthracyclines are being re-evaluated in two directions, identification of biomarkers that predict greater benefit, and applying lower-toxicity formulation. Cardiotoxicity, and the development of secondary leukemia or myelodysplastic syndrome are the utmost concerns with anthracycline prescription in early breast cancer. Change from doxorubicin to epirubicin raises the threshold resulting in cardiotoxicity. In an overview of 19 randomized clinical trials involving 7,110 patients treated with epirubicin-containing regimens, 8-year cumulative probability of AML/MDS was 0.55% (95% CI, 0.33% to 0.78%).

Doxorubicin is still one of the most important chemotherapeutic agents in the management of breast cancer, with very comprehensive and complete over 20 year follow up data. Pegylated liposomal doxorubicin (PLD) is the only logical substitute with confirmed efficacy, or even increased efficacy because single agent PLD is still efficacious in a subset of anthracycline resistant tumors; it has decreased and almost negligible cardiac toxicity, and with its special formulation and pharmacokinetic characteristics, which slowly releases the doxorubicin into the circulation.

A Taiwanese, multi-center, prospective adjuvant PLD study was conducted to evaluate the disease-free survival (DFS) in the two randomized arms, LC vs. EC, in chemotherapy-naive Her2-negative patients with stage I or II breast cancer. The results showed that 2-year DFS and OS rate are comparable between LC and EC treatment arms. The major events in the LC arm were mucosal and dermatologic toxicities, whereas in the EC arm, were hematological problems and alopecia. Most of the patients in the LC arm have better QoL of symptom scale compared to EC. LD0914 is the first prospective, randomized study supporting the efficacy of PLD as adjuvant treatment of early breast cancer patients. Five-year survival results are awaited.