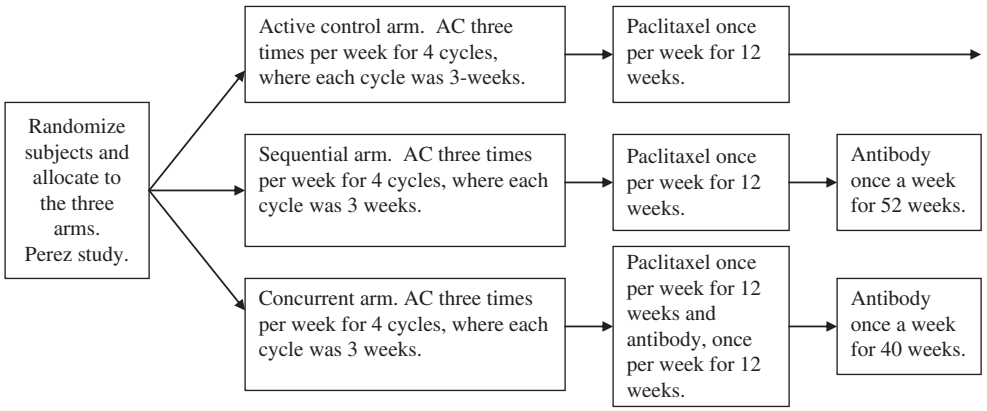

FIGURE 2.5 Schema of a three-arm study. The first arm received an active control treatment. The second arm received small-molecule drug plus antibody on different, nonoverlapping weeks (sequential treatment), while the third arm received small-molecule drug and antibody at the same time, that is, during the same week (concurrent treatment).

the third arm as a concurrent arm (Fig. 2.5). In the control arm, patients received an active control (AC) followed by paclitaxel. The abbreviation "AC" refers to doxorubicin, which is an anthracycline (AC) drug. In the sequential arm, patients received the same drugs as in the active control arm, but followed by an antibody (trastuzumab). In the concurrent arm, patients received the same drugs as in the active control arm, but with the antibody given at the same time (concurrently) as paclitaxel. Trastuzumab (Herceptin®) is an antibody that binds to HER2.

The goal of the study was to determine which treatment was least toxic to the heart. Arm A, which did not include the antibody, was the least cardiotoxic (cardiac damage in 0.3% of subjects). Arm B was more toxic (2.8% cardiotoxic). Arm C was the most toxic (3.3% cardiac damage), but only slightly more toxic than Arm B.

As a general proposition, sequential chemotherapy is preferred over combination chemotherapy, where reducing toxicity is especially needed, for example, with patients who are elderly (54). In other words, toxicity is expected to be a bigger problem where two drugs are administered on the same day, and a lesser problem where two different drugs are administered on separate days. Raetz et al. (55) provide a dramatic example of sequential chemotherapy, but for a different reason. In this study, three different blocks of chemotherapy were administered. Each of these three blocks delivered a different collection of drugs. The goal of using these three blocks of time (nonoverlapping blocks) of chemotherapy was to ensure a lengthy period of remission.

[54]Miles D, von Minckwitz G, Seidman AD. Combination versus sequential single-agent therapy in metastatic breast cancer. Oncologist 2002;7(Suppl. 6):13–9.

[55]Raetz EA, Borowitz MJ, Devidas M, et al. Reinduction platform for children with first marrow relapse of acute lymphoblastic leukemia: A Children's Oncology Group Study. J. Clin. Oncol. 2008;26:3971–8.