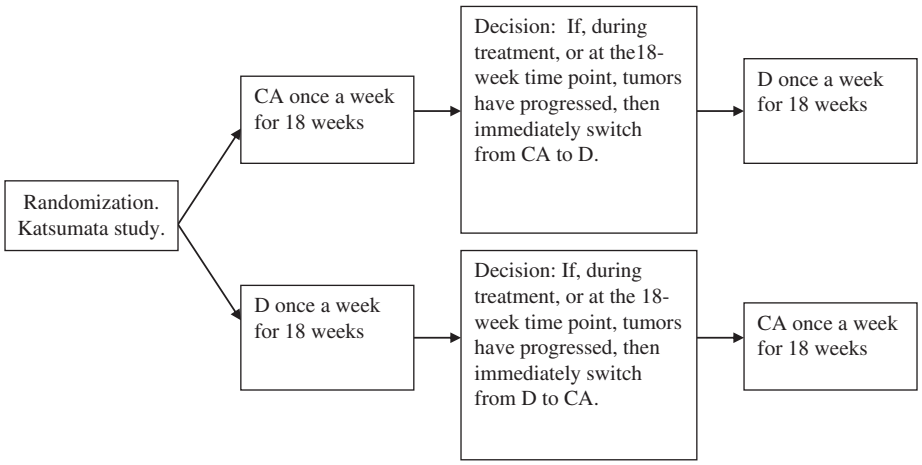

FIGURE 2.13 Schema showing a two-arm study. Each of the two arms incorporated a cross-over design.

k. Decision Tree—The Katsumata Schema

Decision trees occur in the schema of Katsumata et al. (65), where the decision is triggered by an increase (if any) in tumor size (Fig. 2.13). At each decision point, the decision takes the form of crossing over to the alternate therapy, or of continuing with the same type of drug. The letter "A" represents doxorubicin, an anthracycline compound (66). C represents cyclophosphamide. Thus, AC means the combination of doxorubicin plus cyclophosphamide. D represents docetaxel.

The decision to switch drugs was triggered by detection of tumor progression either during the first 18 weeks of treatment or after completion of the first 18 weeks of treatment. In the words of the investigators, "[o]n treatment failure or disease progression during or after treatment, patients were crossed over from AC to D, or from D to AC" (67).

The Katsumata schema shows a cross-over design (Fig. 2.13). Cross-over means that subjects receiving CA therapy, upon encountering the decision tree, were crossed over to D therapy. And subjects receiving D therapy, upon encountering the decision tree, were crossed over to CA therapy. If no tumor progression was detected, then patients were not switched to a different drug. (The clinical trial actually included a third arm, but for clarity in presentation, this arm was omitted from the schema shown below.)

[65]Katsumata N, Watanabe T, Minami H, et al. Phase III trial of doxorubicin plus cyclophosphamide (AC), docetaxel, and alternating AC and docetaxel as front-line chemotherapy for metastatic breast cancer: Japan Clinical Oncology Group trial (JCOG9802). Ann. Oncol. 2009;20:1210–5.

[66]O'Shaughnessy J, Twelves C, Aapro M. Treatment for anthracycline-pretreated metastatic breast cancer. Oncologist 2002;7(Suppl. 6):4–12.

[67]Katsumata N, Watanabe T, Minami H, et al. Phase III trial of doxorubicin plus cyclophosphamide (AC), docetaxel, and alternating AC and docetaxel as front-line chemotherapy for metastatic breast cancer: Japan Clinical Oncology Group trial (JCOG9802). Ann. Oncol. 2009;20:1210–5.