clinical trials, is growth of the tumors beyond a predetermined point. The event where a tumor grows beyond a predetermined point is known as "progression." For any given subject in the placebo arm, at the time that this endpoint is reached, that subject is then crossed-over to the drug (the active treatment) that was used in the study drug arm. Where a cross-over design is used in clinical trials involving a placebo, this design can improve recruitment of subjects in the trial who are not particularly eager to be assigned to the placebo treatment (73,74).

l. Methodology Tip—What Is "Tumor Progression"?

In the clinical trial of Katsumata et al. (75), increases in tumor size were compared to an accepted standard. The accepted standard was as follows: an increase in tumor dimensions of 20% or greater, in the interval between starting chemotherapy and a subsequent tumor assessment.

The term *progression*, in the context of oncology, refers to an increase in tumor size and number, where the increase progresses beyond a certain minimal limit set by these criteria. Progression can be with reference to the RECIST criteria (76,77,78). Some investigators prefer to use an older set of criteria, the WHO response criteria (79,80). The Katsumata study assessed tumors with respect to the WHO criteria.

m. Methodology Tip—Unit of Drug Dose Expressed in Terms of Body Surface Area

The following explains the unit used in the drug dose, "doxorubicin 40 mg/m^2," used above in the study of Katsumata et al. (81). In the words of the investigators, arm A of the clinical trial received, "doxorubicin 40 mg/m^2

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