plus cyclophosphamide 500 mg/m^2 (AC) every 3 weeks for six cycles." The investigators also wrote that patients in arm B of the trial received, "docetaxel 60 mg/m^2 (D), administered by IV infusion over the course of 1 h every 3 weeks for six cycles."

A question that arises is, "What is the meaning of the unit: mg/m^2?"

Drug doses are sometimes expressed in terms of body surface area (meters-squared). According to Felici et al. (82) and others (83,84), many anticancer drugs have a narrow therapeutic window. This means that a small change in dose can lead to poor antitumor effects or unacceptable toxicity. The rationale for using body surface area is to normalize the drug dose among patients. Using body surface area in the unit of drug dosing seems to work best for drugs where there is a relationship between body surface area and a pharmacokinetic parameter, such as the parameter of half-life in the bloodstream.

n. Run-In Period—The Schema of Dy

The schema of Dy et al. (85) discloses a run-in period (Fig. 2.14). Where a clinical trial includes a run-in period, it occurs before randomization of subjects and before allocating subjects to the various arms of the trial.

Run-in periods are used for a variety of purposes, for example, for determining whether patients are willing or capable of taking medications on time, or if patients find the study drug to be intolerably toxic.

As shown in the following schema, the run-in period was used to screen patients for expression of a biomarker, c-kit. Where tumors were negative for c-kit, the subject was not included in the trial. Where tumors were positive for c-kit, patients were included in the trial, and were then treated with imatinib.

While all clinical trials have inclusion criteria and exclusion criteria, whether they be in oncology, infectious diseases, or immune disorders, the clinical trial of Dy et al. (86) is

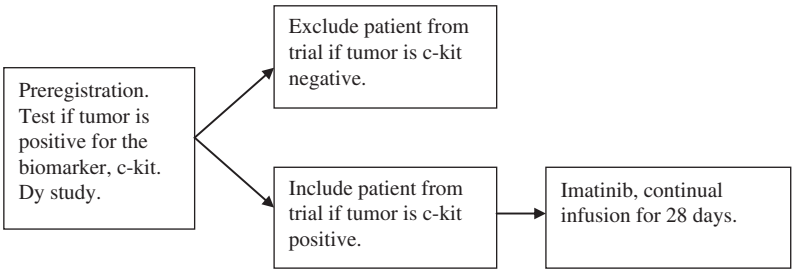

FIGURE 2.14 Study schema of a single-arm trial. The schema includes a run-in period that is used to determine eligibility of each potential subject.

[82]Felici A, Verweij J, Sparreboom A. Dosing strategies for anticancer drugs: the good, the bad and body-surface area. Eur. J. Cancer 2002;38:1677–84.

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[85]Dy GK, Miller AA, Mandrekar SJ, et al. A phase II trial of imatinib (ST1571) in patients with c-kit expressing relapsed small-cell lung cancer: a CALGB and NCCTG study. Ann. Oncol. 2005;16:1811–6.

[86]Dy GK, Miller AA, Mandrekar SJ, et al. A phase II trial of imatinib (ST1571) in patients with c-kit expressing relapsed small-cell lung cancer: a CALGB and NCCTG study. Ann. Oncol. 2005;16:1811–6.