

The question is, therefore, what is the meaning of the unit: mg/m²?

Drug doses are sometimes expressed in terms of body surface area (meters squared). According to Felici et al. (62) and others (63,64) many anti-cancer drugs have a narrow therapeutic window. This means that a small change in dose can lead to poor anti-tumor effects or an 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. (65) 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 if 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 schema in Fig. 2.14, 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.

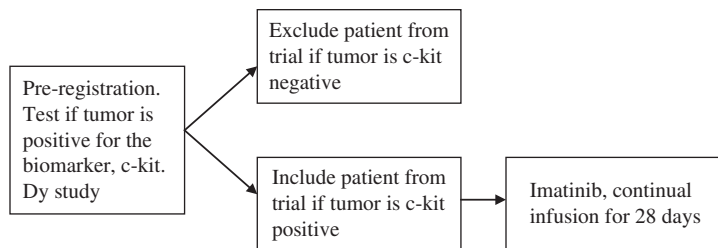


Figure 2.14 Study schema of a 1-arm trial. The schema includes a run-in period that is used to determine eligibility of each potential subject

⁶² Felici A, Verweij J, Sparreboom A. Dosing strategies for anticancer drugs: the good, the bad and body-surface area. *Eur J Cancer*. 2002;38:1677–1684.

⁶³ Sawyer M, Ratain MJ. Body surface area as a determinant of pharmacokinetics and drug dosing. *Invest. New Drugs*. 2001;19:171–177.

⁶⁴ Kouno T, Katsumata N, Mukai H, Ando M, Watanabe T. Standardization of the body surface area (BSA) formula to calculate the dose of anticancer agents in Japan. *Jpn J Clin Oncol*. 2003;33:309–313.

⁶⁵ 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;16:1811–1816.