a drug with a small demonstrated separation between its useful and undesirable dose ranges. In these cases, the recommended starting dose might best be a low dose exhibiting a clinically important effect in even a fraction of the patient population, with the intent to titrate the dose upwards as long as the drug is well tolerated.

Phase II trials are sometimes divided into Phase IIa trials and Phase IIb trials. In the Phase IIa trial, the drug is tested in a small group of (12–100) subjects. In this context, the drug may be used only at a single high dose, that is, at the maximally tolerated dose. In the subsequent Phase IIb trial, several dose levels may be tested (dose-ranging studies) in order to define the minimally effective dose and also to decide the optimal dose, based on efficacy and safety (9).

The final stage of drug development is the Phase III clinical trial. Phase III clinical trials confirm the dose level, frequency, and timing of doses. Phase III trials can involve up to several thousands of subjects. This large number of subjects is needed to ensure detection of less-frequently arising drug-related toxicities, to acquire a confident assessment of efficacy, and to serve as a basis for the package insert or the drug label (10).

II. STUDY DESIGN

Clinical studies take various forms. At its simplest, one person takes a drug, and the person's response to the drug is measured. The response can take the form of various parameters, such as blood pressure, data from an electrocardiogram (11) and titer of a given bacterium or virus, where these parameters are measured shortly before, as well as after, taking the drug.

Small clinical trials generally focus on the pharmacokinetics (PK) of a drug, the influence of food on the PK of the drug, the dose providing the greatest efficacy, and the most appropriate route of dosing. Regarding the dosing route, drugs may be administered orally (per os), intramuscularly (im), intravenously (iv), subcutaneously (sc), rectally, or by inhalation.

Large clinical trials include one or more study arms. For example, a 2-arm clinical trial can take the form of a study drug group and a placebo group. Also, a 2-arm clinical trial can take the form of a study drug group and an active control group. The term "active control" usually refers to an older drug that has been the standard of care for the disease of interest. Moreover, a 3-arm clinical trial can include a study drug group, placebo group, and active control group. The terms placebo and active control are further defined below. Other features of clinical trial design include a run-in period and a follow-up period. Large clinical trials focus on safety and efficacy, but other types of

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[10] Tamimi NA, Ellis P. Drug development: from concept to marketing! *Nephron Clin Pract*. 2009;113:c125–1231.
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