were randomized to receive either placebo or study drug. In the words of the researchers, "[t]he rationale behind the run-in phase was to ensure that the 4 groups would be roughly equal [in size] after 3 years, such that women taking hormone replacement could be compared with women taking. . .combination therapy, or placebo." During the run-in period, 112 potential subjects were discontinued from the trial, where 73 of these were discontinued because of adverse drug reactions resulting from the study drug.

The Greenspan clinical trial is unusual, in that a drug, rather than merely a placebo, was administered during the run-in period. Even subjects eventually randomized to receive placebo received the study drug during the run-in period. Most clinical trials using a run-in period, as part of the study design, use that period to administer only the placebo.

d. To Include Only Study Subjects With Controllable Pain

Run-in periods can screen for study subjects with adequate pain control. In a study of breast cancer by Blum et al. (11), subjects were first entered in a 1-week run-in period, during which subjects were assessed for adequate pain control. Subjects with no pain or with stable pain intensity were allowed to continue with the clinical study. Similarly, Burris et al. (12) included a run-in period in a study of pancreatic cancer in order to exclude subjects who were not able to obtain stable pain. Cartwright et al. (13) included a run-in period, where subjects were assessed for pain control, and where subjects with inadequate pain control were excluded. The run-in period was also used as a convenient time for measuring vital signs, physical measurements, and clinical laboratory tests, all of which were performed within 7 days before start of study drug treatment. In a study by Filiu et al. (14), the run-in period was only used to assess pain, and not to exclude subjects with uncontrolled pain. In the above-cited studies, pain was assessed using the Memorial Pain Assessment scale (15).

e. To Determine the Maximal Tolerable Dose

A run-in period can take the form of a phase I clinical trial, with a first group of study subjects, where a subsequent phase II trial uses a totally different group of study subjects. The goal of this sort of study design is to determine the safety profile of the study drug. In a study of lung cancer, Heymach et al. (16) used a run-in period on a small group of subjects in order to determine the safety profile of two different doses of study drug, that is, 200 mg vandetanib in combination with paclitaxel and carboplatin

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[12]Burris HA, Rivkin S, Reynolds R, et al. Phase II trial of oral rubitecan in previously treated pancreatic cancer patients. The Oncologist 2005;10:183–90.

[13]Cartwright TH, Cohn A, Varkey JA, et al. Phase II study of oral capecitabine in patients with advanced or metastatic pancreatic cancer. J. Clin. Oncol. 2001;20:160–4.

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[16]Heymach JV, Paz-Ares L, Braud FD, et al. Randomized phase II study of vandetanib alone or with paclitaxel and carboplatin as first-line treatment for advanced non-small-cell lung cancer. J. Clin. Oncol. 2008;26:5407–15.