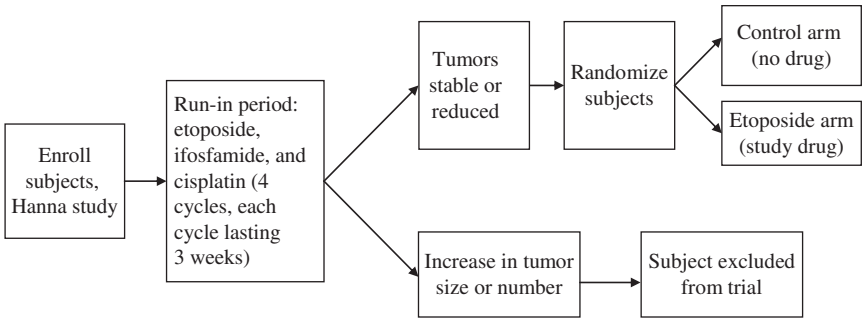

Figure 2.15 Study schema of a 2-arm study that included a run-in period. The run-in period was used to determine eligibility of the potential study subjects

Belani et al. (69) also provide a schema with a run-in period, where the run-in period takes the form of a miniature clinical trial occurring before randomization. In the words of these authors, "[a]fter the completion of two cycles of chemotherapy, patients were reassessed with chest CT to ensure the absence of metastatic progression. In the absence of metastatic progression, patients were randomly assigned to one of two different…regimens." The particular type of trial design used by Hanna et al. (70) Belani et al. (71) is called, "randomized discontinuation" (72). A run-in period in a clinical trial that has a randomized discontinuation feature serves to enrich the study population for patients likely to respond positively to the study drug.

q. How to maintain blinding of the treatment, when the study drug and the control treatment are provided by different-sized pills (or by different volumes of solutions) – the Reck schema

The following concerns studies requiring a "double dummy" design, such as the study of Reck et al. (73) detailed below (Fig. 2.16). This concerns trials with two different

[69] Belani CP, Wang W, Johnson DH, et al. Phase III study of the Eastern Cooperative Oncology Group (ECOG 2597): induction chemotherapy followed by either standard thoracic radiotherapy or hyperfractionated accelerated radiotherapy for patients with unresectable stage IIIA and B non-small-cell lung cancer. *J Clin Oncol*. 2005;23:3760–3767.

[70] Hanna NH, Sandier AB, Loehrer Sr, PJ et al. Maintenance daily oral etoposide versus no further therapy following induction chemotherapy with etoposide plus ifosfamide plus cisplatin in extensive small-cell lung cancer: a Hoosier Oncology Group randomized study. *Ann Oncol*. 2002;13:95–102.

[71] Belani CP, Wang W, Johnson DH, et al. Phase III study of the Eastern Cooperative Oncology Group (ECOG 2597): induction chemotherapy followed by either standard thoracic radiotherapy or hyperfractionated accelerated radiotherapy for patients with unresectable stage IIIA and B non-small-cell lung cancer. *J Clin Oncol*. 2005;23:3760–3767.

[72] Fu P, Dowlati A, Schluchter M. Comparison of power between randomized discontinuation design and upfront randomization design on progression-free survival. *J Clin Oncol*. 2009;27:4135–4141.

[73] Reck M, von Pawel J, Zatloukal P, et al. Phase III trial of cisplatin plus gemcitabine with either placebo or bevacizumab as first-line therapy for nonsquamous non-small-cell lung cancer: AVAil. *J Clin Oncol*. 2009;27:1227–1234.