the advantage of limiting the number of patients exposed to the candidate compound, as a "stopping rule" may end the trial early. This trial design can be advantageous if there is a risk of serious side effects, as it minimizes the number of patients exposed to potential new treatments. Evaluating an expensive candidate compound in a staged clinical trial also decreases the financial risk, as there is less capital outlay required to determine if additional expenses are warranted.

In many case, it is necessary to generate more data than can be provided in a single arm trial. If, for example, the level of response that will be elicited by a candidate compound is not well understood, incorporating a control group in the trial will provide a strong basis for comparison. A two armed, randomized phase II trial with one group receiving the candidate compound and a control receiving either a placebo or the standard of care can provide significant insight (Figure 9.15). The progression and results

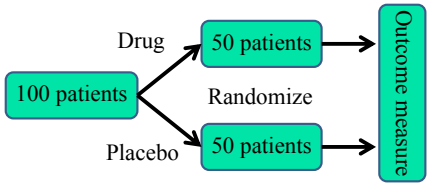

FIGURE 9.15 In a two armed, randomized phase II clinical trial, the patients receive either the drug substance or a placebo. Multiple treatment arms can be included if necessary.

from each arm of the trial can be used to optimize the design of phase III studies. It is also possible to monitor the rate of patient recruitment as the trial progresses. This will provide a sense of how long it might take to recruit a larger population of patients that will be required for phase III clinical trials, as well as any other logistical problems that may occur through the course of the trial. Although the patient population will not be large or diverse enough to definitively determine whether or not a new therapy is suitable for marketing, ideally it will be large enough to extrapolate the number of patient that will be required for the phase III trials. It is also worth noting that this trial design can be extended to include multiple treatment arms in order to determine the optimal dose for phase III trials. In addition, a staged trial design can also be employed in a similar manner to that described above (Figure 9.16).

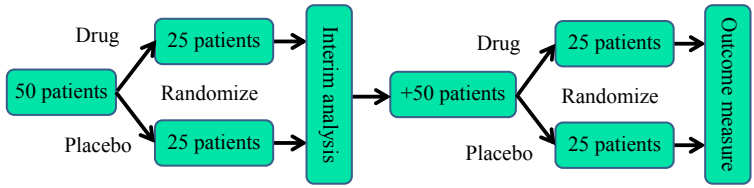

FIGURE 9.16 A two armed, randomized phase II clinical trial can be staged. Results from an interim analysis determine whether or not new patients enter the trial.