phase I trials. A phase II clinical trial for a chronic indication, for example, could be as long as 6 months. All of the patients must be carefully monitored to identify any potential safety risks that might become apparent as the candidate compound is used for longer and longer time periods.

The ability of a phase II clinical trial to arrive at successful conclusion is dependent not only on the candidate compound, but also the trial design and outcome measures that define success. The choice of trial design and outcome measure is highly dependent on the disease or condition that is being examined. A phase II clinical trial designed to determine whether or not an antibiotic is suitable for further clinical study (e.g., phase III clinical trials) will be very different from a phase II clinical trial designed to determine whether or not a candidate compound might be useful for the treatment of migraine headaches or cancer. The complexity of trial design and possible clinical endpoint is far beyond the scope of this text, but an understanding of some of basic trial designs and outcome measures can provide some perspective on the capabilities and limitations of each.

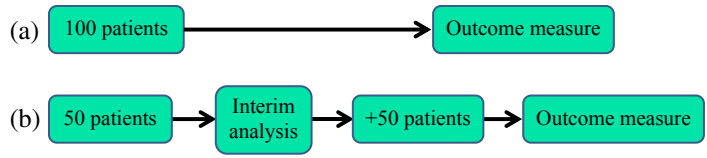

FIGURE 9.14 (a) In a simple single arm phase II study, all patients receive the clinical candidate. (b) In a staged, one arm, phase II study, one group of patients receives the candidate and the results are analyzed. If the interim analysis meets a predetermined goal, the remainder of the patients receive the candidate compound and the trial proceeds. If the predetermined goals are not met, the trial is terminated.

The simplest trial design is a single arm study (Figure 9.14(a)).[40] In this scenario, all of the patients are provided with the new treatment and monitored over time to determine whether or not the treatment is effective. This study design can be cost-effective when compared to more complex designs, as all of the resources are focused on a single patient group. The absence of a control group, however, prevents direct comparison with either a placebo or a standard of care patient group. This is a significant limitation, especially if it is unclear what effect the candidate compound will have on the disease state (e.g., a compound with a novel mechanism of action).

A single arm study can also be designed as a staged study in which a subset of the full group is treated with the candidate compound (Figure 9.14(b)). If the number of patients responding to the new treatment meets a predetermined goal, then the remaining subjects are recruited and the phase II trial continues to its planned end point. On the other hand, if the number of positive responders fails to meet the predetermined objective or a significant safety issue occurs, then the trial is halted. The staged trial design has