

Short course title: Sequential Statistical Methods in the Design and Analysis of Clinical Trials

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Abstract: Clinical trials are experiments testing therapeutic drugs (or treatments) on human subjects. Statistically, design of such a trial must at least satisfy the constraints on type I and type II error probabilities. Mainly due to ethical considerations, it has become a standard practice that clinical trials are monitored periodically by employing interim analysis methods known as sequential testing procedures. Such a procedure, while controlling the type I and type II error rates, may require stopping the clinical trial early before its planned end, if the cumulated data show the drug to be harmful to (or effective in treating) the patients. Focusing on phase II and III clinical trials, in this short course, we will first review some basics concerning a clinical trial, such as choosing an endpoint for monitoring, selecting a test statistic, computing the sample size and making inference on the endpoints for a fixed-size test. We then move on to present various approaches to determine stopping boundaries in designing a sequential clinical trial, including methods of Simon for phase II trials, and Haybittle-Peto, Pocock, O'Brien-Fleming, and the general, more flexible error spending function approach of Lan and DeMets for phase III trials. Terminal (upon stopping of the trial) inference methods will also be discussed such as construction of point estimates, confidence intervals and p-values.