Bayesian Clinical Trials

Brief introduction to phase I and phase IIA trials

Phase I study

- Goal: -Key elements:

Rule based designs

- Traditional 3+3 design

Model based

An alternative to the rule-based methods for finding the MTD is to assume that there is a monotonic dose-response relationship between the dose and the probability of DLT for patients treated at that dose; see Figure 3.4. In this approach, a dose-toxicity curve as well as the TTL are explicitly defined. The goal for the phase I clinical trial is, through treating patients in a dose escalation fashion, to seek a suitable quantile of the dose-toxicity curve; specifically, a dose that will induce a probability of DLT at a specified target toxicity level. This method is most conveniently carried out under the Bayesian framework. Simple one- or two-parameter parametric models are often used to characterize the dose-toxicity relationship, with the Bayesian posterior distribution used to estimate the parameters. These designs use all the data to model the dose-toxicity curve, and provide a credible interval for the MTD at the end of the trial.

Phase II studies

- Phase IIA (single arm) and Phase IIB (multi-arm)
- multistage (Multi-stage designs are useful here for early stopping due to lack of e???cacy should the interim data indicate that the study drug is ine???cacious)

Phase IIA designs

To provide an initial e???cacy assessment, a phase IIA trial is often designed asasingle-arm,open-labelstudythatrequirestreating40to100patientsin a multistage setting. Multi-stage designs are useful here for early stopping due to lack of e???cacy should the interim data indicate that the study drug is ine???cacious.

- ▶ Simon optimal design

Getting the slides

- The slides for this course were created with Rmarkdown: `http://rmarkdown.rstudio.com/`.
- They are available from `https://github.com/berkeley3/bayesianCT-course`.
- To re-compile the slides:
    - Download the directory containing the lecture from Github
    - In R open the .Rmd file and set the working directory to the lecture directory
    - Click the *KnitHTML* button on Rstudio or run the following commands:

```r
library(rmarkdown)
render("index.Rmd")
```