**Thall, Homework assignment #2 for Stat 630, Spring Semester, 2012.**

**Answer each question precisely and completely. Be as brief as possible, but clearly define any notation before using it. Use clear, complete sentences when giving your answers and derivations. You may use any references you like, but all of your work must be your own. This homework assignment is due at the start of class, Tuesday, March 13.**

Apply the Thall-Simon Estey (1995) method to design the following trial. Use the computer program “multc99” available from <http://biostatistics.mdanderson.org/SoftwareDownload>

1. A single-arm phase II clinical trial of the experimental preparative regimen intravenous busulfan + clofarabine for allogeneic bone marrow transplantation for treatment of acute leukemia is to be conducted. Patients are in first remission and have a matched related donor. The anticipated accrual rate is 20 patients per year. A trial with three years of accrual is planned. The five patient outcomes of interest, for the purpose of interim monitoring, all scored within the first 30 days, are as follows:

|  |  |  |  |
| --- | --- | --- | --- |
| ALIVE | | | DEAD  (50) |
|  | Toxicity | No Toxicity |
| Engrafted | E and T (50) | E and No T (100) |
| Not Engrafted | No E and T (20) | No E and No T (30) |

The counts of the 5 events using the historical “standard” preparative regime S are given in the cells in parentheses.

1. Summarize the disease, treatment, outcomes, and probability model (likelihood and prior for both the experimental and standard regimens).
2. Construct a design with early stopping rules to monitor
3. Pr(Death), with no slippage
4. Pr(Engrafted), targeting an improvement of .15
5. Pr(Toxicity), allowing a slippage of .05
6. Construct a set of six scenarios for simulation study.
7. Under each scenario, examine three designs with a maximum sample size of N= 60 and cohort sizes of 5, 10, or 20. For each design, calibrate the design’s stopping rule parameters so that the design has good overall properties. For each design, give the final stopping rules explicitly.
8. For one selected scenario, with a cohort size of 10, do a sensitivity analysis in maximum sample size N= 40, 50, 60, 70, 80.

2. Now construct a greatly simplified design by defining Success = [alive and engrafted without toxicity at day 30] and using ONE futility monitoring rule for Pr(Success). Give the probability model and method for this simplified design, simulate it under three scenarios, and do a sensitivity analysis in maximum sample size as in 1e above.