Targeted Phase I Oncology Trial

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1. Objective
Develop a modeling approach to explore the operating characteristics of a Bayesian Phase I oncology trial design that enriches enrollment with patients bearing a mutation that favors response.

2. Model/Assumptions
A clinical trial is considered where patients are assigned to doses in order to efficiently infer the Maximum Tolerated Dose using a Bayesian methodology. It is assumed that each patient also provides an efficacy estimate. The trial design enriches enrollment with patients bearing a mutation that favors response.

2.1. Objective
design that enriches enrollment with patients bearing a mutation that favors response.

2.2. Model/Assumptions
A simulation analysis is conducted to explore the operating characteristics of a go/no-go decision rule based on estimating tolerability and efficacy concurrently while enriching the study population with better responders. Patients with a gene mutation are assumed to respond better to the new oncological agent.

2.3. Results/Discussions

3. Results/Discussions

3.1. Results show that increasing ER typically will improve the efficacy inference and the accuracy of the Go decision; however, the incremental benefit of increasing ER is diminishing and the diminishing rate depends on precision of the measurements of efficacy/safety and points and mutation prevalence. Refer to Fig. 3.1-3.2.

3.2. The average total recruitment time increases with ER, and the lower the MF the higher the rate that recruitment time increases with respect to ER, which is illustrated in Fig. 3.3.

4. Conclusion
The simulation model developed provides guidance in decision-making to go for targeted Phase I oncology trial in terms of cost and time saving, accuracy and precision of parameter estimates and accuracy in predicting development success.

References: