1. Introduction

Recent development of molecular biology and genomics allow to classify patients with a common oncologic disease into the several subpopulations depending on their molecular profiles including biomarker or genotypic feature. To accommodate this growing trend, basket trial which evaluates the efficacy of the targeted therapy based on the corresponding molecular characterization across the cancer types has been operated.

Simon (2017) provided a basic framework of new design that evaluate the posterior probability of the drug activity in the context of Bayesian model averaging, but little is known about the modified method of this design. Here we calculate the posterior probability of the drug activity is calculated based on the assumption that response rates of all subpopulations are equal (or not equal) using the interim data of all the subpopulations during the trial.

However, the response rates are sometimes different among the subpopulations; for example, vemurafenib is active in several histologies with V600E BRAF mutation, but not in colorectal cancer (Chan et al., 2015).

2. Purpose

To accommodate the inconsistency of the drug activity among subpopulations, we propose the modified Simon’s method, and examine the operating characteristics of it by simulation studies.

3. Simon’s basket design

Let \( n_k \) denote the number of patients for stratum \( k \); \( n_0 \) and \( n_1 \) denote the number of response rate in a stratum. Let \( p_0 \) denote the response rate for stratum 0. If \( p_0 \geq p_{	ext{Hi}} \), then the drug is active in stratum 0; and if \( p_0 \leq p_{	ext{Lo}} \), then the drug is inactive in stratum 0.

In the Simon’s design (Simon, 2017), given the data \( (r_1, r_2, \ldots, r_j, n_0, n_1) \) at that time, the posterior probability of the drug activity \( \text{Pr}(p_1 | n_0, n_1) \); and it is defined as

\[
\text{Pr}(p_1 | n_0, n_1) = \frac{\binom{n_0}{r_0} \binom{n_1}{r_1} \beta(p_0; n_0, n_1) \beta(1-p_0; n_0, n_1)}{\binom{n_0}{r_0} \binom{n_1}{r_1} \beta(p_0; n_0, n_1) \beta(1-p_0; n_0, n_1) + \binom{n_0}{r_0} \binom{n_1}{r_1} \beta(p_1; n_0, n_1) \beta(1-p_1; n_0, n_1)},
\]

where \( \beta(p; n, m) \) denotes the binomial distribution with parameter \( p \) and \( \lambda \) the posterior probability of \( H_0 \), and 1-\( \lambda \) is the prior probability of \( H_1 \).

4. Modified method

We propose the homogenous probabilities of the response rates between subpopulations and the calculating method of the posterior probability of the drug activity based on the homogenous probabilities. Specifically, we calculate the posterior probabilities of the response rates between subpopulations, then divide the subpopulations into the homogenous subgroups based on the homogenous probabilities. We calculate the posterior probabilities of the drug activity based on the homogenous subgroups.

5. Simulation studies

5.1 Simulation Settings

The procedure of each simulation experiment is based on that of the Simon R (2017). We denote \( N_{\text{max}} \) the maximum sample size of the trial, and \( n_k \) is the number of interim analyses. \( N_{\text{Hi}}=1 \) and \( N_{\text{Lo}}=20 \) from Equation (1). If \( \text{Pr}(p_1 | n_0, n_1) \) is set to be greater than 0.50, then the drug is taken to be active; otherwise, the study should be rejected. If we continue to enroll patients to the stratum \( k \), then we define the posterior probability of the drug activity from Equation (1) to Equation (3).

5.2 Results

We evaluated the results of \( TP, FP, TN, FN \) under other conditions (The results are not shown). The results when \( N_{\text{max}}=100 \) were similar to the results when \( N_{\text{max}}=50 \). The number of patients per stratum in each trial is set to be 30. The number of patients in a homogenous subset \( j \) is \( n_{\text{Hi}}, n_{\text{Lo}}, n_{\text{Med}} \), respectively.

The other procedures are same as those of the Simon’s method.