Reviewer’s report

Title: How to design a dose-finding study using the Continual Reassessment Method

Version: 0 Date: 08 Jan 2018

Reviewer: Akihiro Hirakawa

Reviewer's report:

This paper aimed to provide comprehensive recommendations for use of the continual reassessment method (CRM) in phase I trials, but those provided were based solely on results that have been reported in the literature. Because the viewpoint of this paper is unique and novel to some extent, the addition of new recommendations for the CRM proposed by the authors would increase the value of this paper.

Major comments

Many researchers have examined the operating characteristics of the CRM in phase I trials that determine the recommended phase 2 dose of an investigational drug as monotherapy use and provided recommendations for the use of CRM in practice. The recommendations given in this paper are similar to those. In order to enhance the contribution of this work, the authors should add these points, if possible: i) the CRM with EWOC, ii) bivariate CRM using toxicity and efficacy outcomes (mostly for molecularly targeted agents), or iii) time-to-event CRM.

The manuscript summarizes the results obtained by the literature and does not provide new recommendations proposed by the authors. Please clarify what the recommendations by the authors are with respect to the specifications of all the elements of CRM (i.e., TTL, model, skeleton choices, cohort size, sample size, and so on).

It would be useful for readers to provide the practical guidelines/policies based on the experiences of using the CRM in the authors' institutions in addition to the recommendations based on the literature. Furthermore, the discussion about the differences between them would garner clinicians/biostatisticians attention.

Minor comments

Effect of the value of intercept in the one-parameter logistic model on the operating characteristics of the CRM should be discussed.
The authors should clearly state the situations where the informative and non-informative prior distributions are recommended in general.

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