A new adaptive design for Phase II clinical trials

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In a Phase II trial for a new treatment in locally advanced stage IIIA/B Non Small Cell Lung Cancer, a series of challenging questions have arisen, leading to consider a new adaptive Phase II design. Namely, the aim was to examine as primary endpoint the 6-month pneumonitis-free rate of grade ≥ 3 for patients with Non Small Cell Lung Cancer under the new treatment. The design, for safety reasons, should also have an interim analysis based on the 3-months pneumonitis-free rate of grade ≥ 3, i.e. a different, but clearly related to the primary, endpoint. This creates some important issues. First of all the endpoint used is discrete, taking, usually, in such Phase II designs, small integer values, and hence we need to derive the appropriate boundary values to achieve correct alpha. Moreover, one needs to take into account the fact that the response used in the interim and the final analysis is different (but related). We work with an appropriately defined bivariate binomial distribution in order to split the alpha and define the sample size needed. The properties of the proposed design are described. Optimal designs are also considered. The relationship of this approach to similar problems in seamless adaptive designs are discussed.

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