Abstract

Drug development requires a series of complex decisions, many of which depend on rigorous statistical methodology. This thesis, carried out in collaboration with Chiesi Farmaceutici S.p.A., contributes three new methodological advances addressing challenges in trial planning, randomisation, and bioequivalence assessment. The first contribution examines how prior knowledge can be incorporated into trial design through the *probability of success* (PoS). We introduce the notion of PoS *post interim* — defined conditionally on the Data Monitoring Committee's recommendation to continue the trial following an interim analysis — and characterise its formal relationship with the classical PoS. By analysing how efficacy and futility boundaries influence these probabilities, we provide insights that support boundary selection and enhance the interpretation of interim decisions. The second contribution focuses on response-adaptive randomisation in multi-arm phase II trials. Building on weighted information-theoretic principles, we develop a Bayesian randomisation method for normally distributed outcomes with unknown means and variances. The design favours treatments aligned with clinically desirable profiles while preserving sufficient allocation to control, and it balances exploration and exploitation through tunable parameters. Extensive simulations compare the method against established alternatives. The third contribution concerns power calculation in bioequivalence studies — an application that relies on the multivariate non-central t distribution. We clarify inconsistencies in the literature on the definition of the non-central t and and provide the correct expression for power. We then apply this result to improve blinded sample-size reassessment, incorporating (blinded) interim information on both variance and means. Together, these contributions offer theoretical and practical advances that support more efficient and informative drug development.