A forward looking covariate-adjusted response-adaptive (CARA) patient randomisation rule: delivering personalised treatments, patient benefit and power gains in multi-armed trials

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Abstract

Over the past few years, personalised medicine (understood as the tailoring of medical treatment to the individual characteristics of each patient) has shown promise through the approval of new cancer therapies for patients with specific genetic mutations. Delivering personalised treatment in the current context of drug development poses several challenges. For instance, when there exist several promising new treatments and relatively few patients to test them, even fewer patients when a treatment works only within a biomarker subgroup. Novel methodology for trial design that is able to identify superior treatments more quickly, mainly treatments that work better within subgroups, is an essential requirement to make personalised medicine possible.

In this talk I will present a covariate-adjusted response-adaptive (CARA) rule recently introduced in Villar & Rosenberger (Covariate-adjusted response-adaptive randomization for multi-arm clinical trials using a modified forward looking Gittins index rule, Biometrics Volume74, Issue 1 March 2018 Pages 49-57). The resulting randomisation rule has the following properties: a) it is non-myopic, i.e., it adapts randomisation probabilities considering not only past observations but also potential future patient randomisations and their outcomes; b) it is nearly optimal from a patient outcome perspective, tending to randomise more patients into the superior arm when this exist (even if the superior arm differs according to a covariate profile); c) it is computationally tractable and d) it correctly identifies with a high probability superior treatments in subgroups of patients after relatively small number of patients have been treated. I will also discuss how this procedure has resulted from an attempt of bringing optimisation (bandit theory) closer to clinical practice while providing an answer to the current challenges of therapy development for rare diseases and personalised medicine.