

Bayesian response-adaptive designs for basket trials

LORENZO TRIPPA¹, Steffen Ventz², William T. Barry¹, Giovanni Parmigiani¹

¹*Harvard University, School of Public Health, USA*

²*University of Rhode Island, USA*

Abstract

We develop a general class of response-adaptive Bayesian designs using hierarchical models, and provide open source software to implement them. Our work is motivated by recent master protocols in oncology, where several treatments are investigated simultaneously in one or multiple disease types, and treatment efficacy is expected to vary across biomarker-defined subpopulations. Adaptive trials such as I-SPY-2 (Barker et al., 2009) and BATTLE (Zhou et al., 2008) are special cases within our framework. We discuss the application of our adaptive scheme to two distinct research goals. The first is to identify a biomarker subpopulation for which a therapy shows evidence of treatment efficacy, and to exclude other subpopulations for which such evidence does not exist. This leads to a subpopulation-finding design. The second is to identify, within biomarker-defined subpopulations, a set of cancer types for which an experimental therapy is superior to the standard-of-care. This goal leads to a subpopulation-stratified design. Using simulations constructed to faithfully represent ongoing cancer sequencing projects, we quantify the potential gains of our proposed designs relative to conventional non-adaptive designs.