ABSTRACT

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As adaptive clinical trials (ACTs) receive growing attention and exhibit promising performance in practical trials during last decade, they also present challenges to drug supply chain management. As indicated by Burnham et al. (2015), the challenges include the uncertainty of maximum drug supply needed, the shifting of supply requirement, and rapid availability of new supply at decision points. To facilitate drug supply decision making and the development of mathematical analysis tools, we propose two trial supply chain optimization problems that represent different mindsets in response to trial adaptations. In the first problem, we treat the impacts of ACTs as exogenous uncertainties and study important aspects of trial supply, including drug wastage, resupply policy, trial length, and costs minimization, via a two-stage stochastic program. In the second problem, we incorporate the adaptation rules of ACTs with supply chain management and numerically study the impact of joint optimization on the trial and drug supply planning through a mixed-integer nonlinear program (MINLP). For solution approaches to the problems, we use progressive hedging algorithm (PHA) and particle swarm optimization (PSO) respectively, and take advantages of the problem structures to enhance the solution efficiency. With case studies, we see that the proposed models capture the features of ACT drug supply and the mechanisms of trial conduction well. The solutions not only reflect the impact of trial adaptations but also provide managerial suggestions, e.g. the prediction of needed production amount, the estimation of storage capacity at clinical sites, and the performance of resupply schemes. The joint optimization also suggests a new angle or research extension in the field of ACT design and supply.