Considerations on the mechanics and sample sizes for early trials of targeted agents and immunotherapy in oncology

Read article on trial design and sample sizes for early trials

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ABSTRACT

Introduction: Precision medicine is impacting clinical practice and drug development in oncology, promoting notable changes in the design of early-phase cancer trials. There is increasing pressure on sponsors and clinical trialists to strike the right balance between speed and reliability in the design and implementation of such trials, which now commonly assess activity in expansion cohorts.

Areas covered: We discuss methodological issues related to trial design and sample sizes for phase 1 trials with expansion cohorts and phase 1/2 trials. We review the pertinent literature, present fictitious cases to illustrate the different designs, and discuss their advantages and disadvantages, with a focus on randomized designs in which an experimental and a control treatment are assessed.

Expert Opinion: Designing a phase 1 trial with expansion cohorts requires statistical input and explicit consideration about interpretation of future results. There is currently insufficient emphasis on the role of randomization in expansion cohorts and phase 2 components of early-phase trials. The results from single-arm cohorts may be misleading due to selection bias, but comparative randomized trials may not be feasible in many cases due to budget constraints or ethical arguments. Randomized, non-comparative trials with a control arm used for calibration of historical results are an interesting intermediate solution between single-arm expansion cohorts and randomized comparative studies.

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EXPERT REVIEW OF PRECISION MEDICINE AND DRUG DEVELOPMENT:
https://doi.org/10.1080/23808993.2021.1915693 – Taylor and Francis Group