Objectives, design considerations and endpoint selection for

Phase II clinical trials

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Abstract
Phase II clinical trials are an essential aspect of drug development that enables the "go-no go" decision to be made in order to advance a new agent to Phase III testing. The primary goals of Phase II trials are to estimate drug activity, describe toxicity, develop pharmacokinetic-pharmacodynamic (PK-PD) correlations, and confirm drug-target interactions. This presentation will review the essential elements of a Phase II trial including development of the primary objective and selection of the primary study endpoint, choice of the study population and description of the intervention to be studied. With the increasing number of targeted agents in clinical development, there is increasing use of time to event endpoints in Phase II clinical trials. The pros and cons of such endpoints will be described. Controversy exists regarding the relative merits of single arm and randomized Phase II trial designs. Examples of such designs will be provided and the circumstances in which each type of trial might be preferred will be described. Enrichment designs, such as biomarker-driven clinical trials and the randomized discontinuation design, provide opportunities to enrich the study population with individuals most likely to benefit from the treatment or to display the endpoint of interest. The merits and liabilities of such study designs will be described. At the conclusion of this presentation, participants should have an in-depth understanding of the design options for Phase II trials and should be able to select the optimal design based on the characteristics of the drug being studied, the clinical hypothesis being evaluated and the patient population being enrolled.

Key Messages

• The goals of Phase II trials are to estimate activity, describe toxicity, develop PK-PD correlations and confirm drug-target interactions.

• The optimal trial design will depend on the patient population being studied, the primary endpoint selected, the level of activity of interest, the precision of the estimate of activity.

• Assessment of disease progression depends on definition of progression and extent and frequency of evaluation but is always an estimate as true progression occurs between observations.

• Randomized Phase II designs reduce selection bias, improve patient comparability, and are generally preferred for progression-based endpoints and when historical data are unavailable or unreliable.

References
2. Sharma, et al., JNCI 2011;103:109.3