Session 5: Clinical development

Phase II Clinical Development: Strategy for a robust Phase II program

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Phase II clinical trials are conducted to investigate a drug's therapeutic efficacy and relative safety in patients. Typically these trials are well-controlled, closely monitored, and conducted in a group of patients who are selected by relatively narrow criteria. Most trials in this phase can be classified as therapeutic exploratory. At the minimum, phase II trials should generate enough data to strongly suggest, if not prove, efficacy and identify the most common side effects.

Two of the most important goals of a successful Phase II program are Proof-of-Concept and dose optimization. These goals are not necessarily distinct as an important objective of many early studies in Phase II is often an early estimate of dose response which is then confirmed in later trials. Other important objectives of Phase II trials are evaluation of study endpoints, therapeutic regimens and target populations (e.g. mild vs. severe disease). Exploratory analyses and multiple endpoints may be used to best advantage in this phase of testing.

It is common to divide Phase II trials into IIa and IIb. These trials are different is scope, size and often rigor of design. Surrogate markers for efficacy, e.g. objective measures of skin function obtained using biophysical measurement methods, may be built into designs of Phase IIa trials with fewer patients and only one or two sites. However, in later Phase II studies it is important to choose and validate, if necessary, clinical scores and patient reported outcomes (PROs) which will be used for pivotal studies. In particular, Phase IIb can be defined as a learning phase which lays the groundwork for confirmation in Phase III.

There are many advantages of a robust Phase II program: The indication and inclusion/exclusion criteria for Phase III can be justified by Phase II outcomes. Outcome measures for pivotal studies can be optimized. Safety parameters for Phase III may be better defined, possibly with reduced need for post-marketing risk management and labeling restrictions. Further, there is a lower risk of the necessity of formulation changes in Phase III which may lead to repeated or bridging studies from earlier phases.