Less is more: Dose-response in preclinical xenograft experiments

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Xenograft experiments play an important role for in vivo cancer research. In these animal experiments, tumor cells are transplanted into mice and the growing tumor is measured over time in different parallel groups. Up to know, the focus of the experimental design has been on showing a significant treatment effect, i.e., verifying the proof-of-concept. During the "preclinical lifecycle" of a promising substance, rich dose-response data is gathered and can be analyzed by pooling multiple experiments. However, the dose-response knowledge becomes available after a relatively long time span and after a lot of animals are investigated because dose-finding is not addressed in the planning stage.

Can we get the dose-response information -or even more- faster with less animals?

In this talk, the retrospective analysis of three projects is shown and a new design is proposed combining proof-of-concept and dose-response estimation (e.g. MCPMod [1]). In particular, power analyses for both parts are presented based on the available data for a hypothetical experiment with reduced number of animals per group but with increased number of dose levels. In addition, the results of a pilot experiment are illustrated, the impact of the new design is discussed and the feedback from the in vivo researchers is summarized.

[1] Pinheiro J, Bornkamp B, and Bretz F. Design and analysis of dose-finding studies combining multiple comparisons and modeling procedures. J Biopharm Stat. 16, 5 (2006)