Optimal Design for Informative Protocols in Xenograft Tumor Growth Inhibition Models

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Objectives: Tumor size measurements in vivo xenograft experiments are usually taken only during treatment [1], preventing a correct identification of certain parameters of tumor growth inhibition models. Optimal design in the Simeoni model [2] was used to evaluate the importance of including measurements during the tumor regrowth phase in those studies.

Methods: Optimal design was performed for several xenograft experiments [2,3] in treated and control arms, involving different drugs, schedules and cell lines. Sampling design was optimized, for each selected experiment, with or without the constraint of not sampling during tumor regrowth, that we defined as “short” and “long” studies, respectively. In the long study, measurements could be taken up to six grams of tumor weight, for ethical reasons, whereas in the short study the experiment was stopped two/three days after the end of treatment period. Design optimization was performed using the determinant of the Fisher information matrix in PFIM 4.0 [4]. Predicted Relative Standard Errors (RSE) were used to compare those scenarios.

Results: Predicted RSE obtained in long studies were better compared to those obtained in the short study of the corresponding experiments. Indeed, some optimal times were located in the regrowth phase, highlighting the importance of continuing the experiment also after the end of the treatment.

Conclusions: Based on results obtained here, making measurements during tumor regrowth should become a general rule for more informative preclinical studies in oncology.

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References