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Objectives: To explore the capabilities of Simulo (a Java-based software for model-based simulations, running on an R backend with a graphical user interface) in the optimization of oncology clinical trials.

Methods: A pharmacokinetic (PK) bevacizumab models for pediatric and adult populations [1, 2] were implemented in Simulo [3]. Several dosing strategies for pediatrics (body surface area, body weight, tier-based dose) were explored and compared with the exposure (Cmin and Cmax) obtained in adults patients receiving 10 mg/kg every two weeks. Moreover, tumor growth (TG) inhibition metrics and gastric cancer patients baseline characteristics, linked to overall survival (OS) using a time-to-event model, were also implemented [4].

Results: Figure 1 shows the simulation interface. On the left side, the drug model items are displayed, allowing the user to easily review the model implementation. On the right side, Simulo live view was used to look at bevacizumab serum concentration–time profile, dynamics of the TG model and the corresponding survival plots (R-codes can be entered directly in Simulo to customize the plots). Simulations indicated that body weight based dose is the most appropriate dosing for children.

Figure 1. An example of Simulo screenshots

Conclusion: Simulo is a platform that allows pharmacometricians to explore all sorts of model-based simulation scenarios in an intuitive, easy and flexible environment. Its application to complex oncology PK and PD models was demonstrated by this bevacizumab example. The methodology can be extended for other drugs, already approved or in development. Simulo can help to optimize study designs and different dosing schedules, maximizing the probability of success and facilitating go/no-go investment decision-making.

References: