# AbstractID: 13443 Title: A computational tumor modeling framework for the optimization of molecular targeted therapies

**Purpose:** Current treatment schedules of molecular targeted therapies are established through costly clinical trials. Although several dosing schemes are used clinically, optimal dosing regimens remain unknown. We developed a computational tumor modeling framework to compare dosing schedules based on simulated therapeutic response.

**Method and Materials:** A pharmacokinetic/pharmacodynamic model was developed to simulate changes in tumor cell proliferation and vascular function. The model was applied to data from a clinical trial in which patients received sunitinib, a molecular targeted agent with anti-angiogenic and anti-proliferative effects, on a 4/2 (4 weeks on, 2 week break) or 2/1 schedule. Using [$^{18}$F]FLT PET/CT imaging, levels of tumor proliferation and vascular function were assessed at baseline, peak drug exposure, and during treatment break. After testing the model on data from the 4/2 schedule, we compared simulated therapeutic responses for these dosing regimens: 4/2 cycle, two consecutive 2/1 cycles, and continuous dosing.

**Results:** Trends in proliferative response were successfully simulated within one standard error of the population means. Two consecutive 2/1 cycles resulted in a 12% greater decrease in tumor proliferation as compared to one 4/2 cycle due to decreased drug washout during the off-drug period. For iso-response conditions, the dose for the 2/1 schedule could be reduced to 80% of the 4/2 schedule (from 50mg/kg/day to 40mg/kg/day). Continuous dosing using lower daily doses (32.5mg/kg/day) yielded the best growth inhibition after 6 weeks.

**Conclusion:** The implemented model successfully reproduced trends in proliferative response observed in patients receiving sunitinib. Continuous dosing yielded the best growth inhibition, and outperformed two consecutive 2/1 cycles and the 4/2 regimen, indicating that this regimen might be favorable, especially for patients requiring lower daily doses to manage toxic side effects. Upon successful validation, the implemented model could serve as a cost-effective tool to help identify improved drug regimens.