Tumor Growth Inhibition Modeling in First-line Advanced Renal Cell Carcinoma (RCC): an Analysis Across Multiple Types of Treatments

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**Background:** Early prediction of tumor response of patients could support drug development decisions in oncology. Tumor growth inhibition (TGI) metrics estimated based on modeling of longitudinal tumor size data have been shown to be predictive of patients’ survival in a variety of tumor types. TGI modeling across multiple treatments, including combination immunotherapy with a VEGF receptor inhibitor has not been studied. A TGI model was developed to characterize the time course of tumor size across 4 clinical studies and 5 different treatments.

**Methods:** Four Phase 1b or 3 studies were included in the analysis with 5 treatments: interferon-α, sunitinib, sorafenib, axitinib, and avelumab + axitinib. The primary tumor dynamic model took the general form previously described by Claret *et al*. and included cell kill rate constant (KD), growth rate constant (KL) and drug-resistance rate constant (λ) parameters. Treatment and baseline tumor size were tested as covariates at α=0.05 for forward inclusion and α=0.001 for backward elimination.

**Results:** A total of 1839 patients with baseline tumor measurements were included. The final model included the effect of treatment on all 3 parameters and baseline tumor on KD. Relative to sunitinib (reference), interferon-α exhibited 35.5% higher KD, 9% lower KL and 18% higher λ, consistent with the fast decrease in tumor size and shorter durability of response observed. Other TKIs sorafenib and axitinib had generally similar KD, KL and λ. For avelumab + axitinib, KD was 7.7% lower while KL and λ were 9.2% and 6.2% higher, with derived TGI metrics suggesting gradual decrease in tumor size and longer durability.

**Conclusion:** The tumor kinetics from first-line patients with RCC were well characterized and reflected the different treatment modalities.

**Keywords** – RCC, immunotherapy, tumor modeling