Tumor Growth Dynamic Modeling-Applications in Oncology Drug Development, Submission, and Market Access

Co-Chairs
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Description
Model-informed drug development (MIDD) approaches have advanced quickly in recent years. The PDUFA VI has specific commitments to enhance MIDD. Many attempts have been applied to model the tumor dynamics, serving the purpose to accelerate the drug development, to support NDA/BLA filling, and to improve market access (1). One of the commonly utilized MIDD approach is tumor-growth-dynamic modeling (TGD), i.e., tumor growth inhibition, tumor re-growth, and as the surrogate of predicting the survival probability with the treatment.

TGD has been utilized in preclinical and translational stage to select the promising drug candidate, and to assist the pharmacological projection of the starting human dose in FIH trials, and to leverage to the clinical cancer patient data (1). TGD models have also been applied in early and late stages of clinical development (2, 3). During the Phase 1/II stage, TGD can support early clinical decisions, i.e., go/No-go decisions for moving to Phase III, via predicting survival outcomes using the longitudinal tumor size data as the surrogate metrics (4). Additionally, TGD can address the medical concerns in clinical practice, such as the impact of clinical covariates by quantifying the effects of genotype variations on patient response (5). Also, TGD models have been applied to identify the sub-patient populations who would benefit the most (6). Further, models based on tumor growth data obtained from patients can help in deciding on the optimal dose and dosing algorithms.

This symposium aims to illustrate the recent advances, and specific applications of TGD for preclinical and clinical pharmacometricians. Application and impact of TGD approach in drug development will be discussed with case examples in the oncology therapeutic area. Current thinking of regulatory view on TGD will also be shared.

Learning Objectives

- To provide a comprehensive review of the methodology, utilities and recent advances of TGD models, in oncology drug development
- To demonstrate the preclinical and clinical case examples of TGD in oncology drug development
- To provide the regulatory perspective on TGD models in NDA/BLA submissions
Session Speakers and Presentations

Peter Bonate - Comprehensive overview of Tumor-growth-dynamic Modeling: Descriptive and Predictive Power

Scope: will provide overview of the background and current advances of the TGD modeling, and will provide a summary of various published TGD models and their utilities in oncology drug development.

Yan (Summer) Feng - Evaluation of Different Pattern of Tumor Dynamics with Immuno-Oncology (I-O) and Chemotherapy Agents Treatment by Utilizing Mixture Tumor Growth Dynamic Modeling

Scope: will provide the thinking paradigm and case examples of how to analyze the clinical TGD data, for the IO agents, using mixed model approach.

Hongmei Xu - De-convolving Response Evaluation Criteria In Solid Tumors (RECIST) in Non-small Cell Lung Cancer Using a Generalizable Bayesian Tumor Size Model

Scope: will present a case study of TGD using Bayesian approach, and a generalizable Bayesian tumor size model will be applied to RECIST in non-small cell lung cancer.

Jingyu Yu - Applications of TGD Modeling in Regulatory Decision-Making

Scope: will present a survey of the utilities of TGD modeling in NDA/BLA submissions and a case example to highlight the challenges and opportunities from the regulatory point of view.