Value of Model-Based Characterization of Time-Profile of Tumor Lesion Data to Assess Treatment Effect in Patients With Non-Small Cell Lung Cancer (NSCLC)

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Objective: Conventionally, response to treatment of patients with solid tumors is assessed by RECIST criteria, whereby the sum of the longest diameters of index tumor lesions is employed as a measure of the aggregate tumor burden. This measure of response is agnostic to the number of index lesions used to compute the aggregate tumor burden. This analysis investigated the value of describing patients’ tumor lesion level response to treatment, relative to describing the aggregate index tumor burden response.

Methods: Longitudinal tumor lesion data from 426 patients with NSCLC treated with docetaxel were fit to 3 versions of the tumor growth dynamics model of Wang et al [1], describing alternative measures of tumor response: aggregate tumor burden (Model 1), average of the longest diameters of index lesions (Model 2), or longest diameter of each index lesion (Model 3). All 3 models were parameterized in terms of baseline tumor burden/lesion size, shrinkage rate constant (TS), and growth rate (TG). Models 1 and 2 incorporated between patient variability in these model parameters, whereas Model 3 incorporated both between and within patient variability of these parameters.

Results: Table 1 presents the parameter estimates of the 3 alternative models of tumor response. The between patient variability of TS and TG were comparable across the 3 models. However, the within patient variability of TS and TG parameters in Model 3 was higher than the between patient variability.

Conclusions: Between lesion variability in response may inflate the extent of between patient variability in response. Tumor growth dynamic models describing the time-profile of individual lesions may be more sensitive to detecting the effect of treatment than models of aggregate tumor burden

References: