Assessment of Tumor-Size Response Metrics to Predict Progression Free Survival (PFS) in Patients With Second-Line Advanced Breast Cancer (ABC)

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Objectives: To evaluate new metrics of tumor-size response to predict PFS in patients with second-line hormone-receptor positive ABC.

Methods: Tumor size data from 405 patients who received palbociclib plus fulvestrant or placebo plus fulvestrant as 2nd line treatment in a Phase III study were included in the analysis. The tumor-size response metrics estimated from tumor growth inhibition models including growth rate, kill rate, time to nadir, tumor regression at 8, 16, 24 weeks, and time-varying tumor regression (TV) up to 8, 16, 24 weeks (TV8W, TV16W, TV24W) were assessed as univariate using log-logistic models to predict PFS. The best tumor-size response metric and baseline prognostic factors identified in the univariate analysis were subsequently assessed in multivariate models to predict PFS. Model performance was evaluated by comparing the observed PFS versus the predicted PFS for each treatment arm and high/low tumor regression groups separated by median tumor size change using simulations (1000 replicates of the phase III study).

Results: Out of the tumor-size response metrics tested, TV performed best in predicting the PFS. In the multivariate analysis, TV, REGION, and baseline aspartate aminotransferase (BAST) were found to be significant and included in the final model. There was a treatment effect for BAST. Figure 1 shows that using the final model while the model performance improves with the longer observation time, TV16W performed similarly to TV24W in predicting PFS. Although not as good, TV8W also provided reasonable predictions that may be used for early prediction if needed.

Conclusions: A tumor size-survival model was developed to describe the relationship between tumor regression and PFS in second-line ABC. Using the final model, early tumor regression readout, TV8W, TV16W or TV24W, may be used to predict PFS of of new drugs with similar mechanism of action in this indication. At the time of the analysis, all available tumor regression data should be used for the prediction.