An R-Shiny Web Application to Support Early Assessment and Decision Making of Oncology Studies Using Multivariate Tumor Growth Inhibition and Overall Survival Disease Models

Mathilde Marchand¹, Laurent Claret², Wan-Ting Lin², Shang-Chiung Chen², Helen Winter², Sandhya Girish², Jin Y. Jin², René Bruno²
¹ Certara Strategic Consulting, Marseille, France; ² Genentech/Roche, Marseille, France and South San Francisco, CA, USA

Objective
To develop a disease modelling and simulation (M&S) R-Shiny application (Apps) to help assess novel treatments or combinations in comparison to historical control (standard of care (SOC)) during early oncology clinical development.

Methods
The Apps requires a tumor growth inhibition (TGI) population model with covariates effects for SOC and a TGI-Overall survival (OS) model in the tumor type of interest [1]. A bi-exponential TGI model [2] with baseline covariates (e.g., demographics, prognostic factors, inflammatory markers) effects on growth rate (KG) was available. Multiple case examples suggest KG is a good predictor of OS [1, 2]. A multivariate lognormal model of OS was also available with baseline covariates and KG estimates. An interactive application was developed using the RStudio “Shiny” package [3] to explore and compare KG and OS for the combination relative to SOC.

References

Results
In the current example SOC is single agent (SA) therapy. The models were used to assess the benefit of combination treatment on KG adjusted to baseline patients characteristics and project expected OS and benefit (hazard ratio (HR)) relative to SA (Figure 1).

KG estimates for the combination are compared to covariate-adjusted typical SA KG to assess the benefit of the combination on KG (ΔKG). For the current example the benefit on KG is modest (18% slower than SA) (Figure 3).

HR of the combination vs. SA is derived using simulated expected OS. For the current example, the benefit of the combination on OS is small (Figure 4). The user can change some arguments of the simulations to explore the impact on the outcome. Simulated expected HR (N=5000 by group) would be 0.91 [0.87;0.96] for this example. A clinical trial like prediction is given in Figure 4 with 250 patients per group.

Figure 1: Schematics of operations
Figure 2: Exploration of KG or tumor data
Figure 3: Overall ΔKG
Figure 4: Hazard Ratio Simulations using TGI-OS Model