Prediction of SVR rates in HCV GT-3 non-cirrhotic patients with 8 weeks of Daclatasvir + Sofosbuvir ± Ribavirin treatment using a viral kinetics model

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Objectives: Treatment of Hepatitis C virus (HCV) genotype (GT) 3 is more challenging than other genotypes. In the ALLY-3 Phase 3 study, AI444218, 12 weeks of Daclatasvir (DCV) + Sofosbuvir (SOF) demonstrated a 96% sustained virologic response rate at 12 weeks after completion of therapy (SVR12) in HCV GT-3 non-cirrhotic patients. We investigated if HCV GT3 patients would benefit from a shorter treatment duration and the addition of ribavirin (RBV).

Methods: A non-linear mixed effects (NLME) viral kinetics (VK) model was used to reproduce the viral load measurements with 12 weeks DCV+SOF to optimize model parameters. The model included a wild type strain and a drug resistant strain. A Markov chain Monte Carlo (MCMC) Bayesian Laplacian algorithm was used for parameter estimation. Stochastic simulations using the posterior MCMC Bayesian samples were performed to predict SVR12 for 8 weeks for treatment with and without RBV.

Results: The VK model adequately captures the observed SVR12 results for 12 weeks of treatment with DCV + SOF. The model predicted that SVR12 would be 82% for a 8 week DCV+SOF treatment. The addition of RBV is predicted to increase the SVR12 to 96% following 8 weeks of treatment.

Conclusions: A mechanistic population viral kinetics model was used to characterize the 12 week DCV+SOF treatment efficacy data, and then to predict the efficacy of 8 weeks DCV+SOF±RBV treatment. We find that 8 weeks DCV+SOF treatment is suboptimal for HCV GT-3 non-cirrhotic patients, while 8 weeks DCV+SOF+RBV treatment would be expected to be more efficacious.