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The use of viral dynamics modeling to optimize the design of a Phase Ib trial, facilitate its analysis, and inform the decision making for the development of directly acting HCV compounds

Hepatitis C virus (HCV) causes a chronic infection of the liver, and leads to fibrosis, cirrhosis, and in some patients to hepatocellular carcinoma. Current standard of care (pegylated interferon plus ribavirin for 48 weeks) is an arduous regimen for the patient and has a cure rate of only 50 % in genotype 1 (GT 1) patients. Therefore, in recent years there has been significant effort to develop directly acting antivirals that will have a substantially higher rate of cure and require a shorter period of treatment. This presentation will describe how we used pharmacokinetic and viral dynamics modeling to design the duration of treatment in a Phase Ib clinical trial of an HCV NS5B polymerase inhibitor in GT 1a, 1b, and 3 patients, and to determine the optimal sampling times both during and after treatment. Quantitative analysis of the resulting viral load data led to a much clearer understanding of the response across genotypes and supported the decision making process in clinical development.