May 17th, 12:00 PM - 12:30 PM

A mathematical modeling study on HDV RNA, ALT, and HBsAg dynamics reveals dual mechanisms of peginterferon-lambda.

Adquate Mhlanga
The Program for Experimental & Theoretical Modeling, Division of Hepatology, Department of Medicine, Loyola University Medical Center, Maywood, IL, USA, amhlanga@luc.edu

Ohad Etzion
Department of Gastroenterology and Liver Diseases, Soroka University Medical Center, Beer-Sheva 84101, Israel, ohadet34@yahoo.com

Harel Dahari
The Program for Experimental & Theoretical Modeling, Division of Hepatology, Department of Medicine, Loyola University Medical Center, Maywood, IL, USA, hdahari@luc.edu

A mathematical modeling study on HDV RNA, ALT, and HBsAg dynamics reveals dual mechanisms of peginterferon-lambda.

Adquate Mhlanga[1], Ohad Etzion[2], and Harel Dahari[1]

[1]The Program for Experimental & Theoretical Modeling, Division of Hepatology, Department of Medicine, Loyola University Medical Center, Maywood, IL, USA

[2]Department of Gastroenterology and Liver Diseases, Soroka University Medical Center, Beer-Sheva 84101, Israel

Hepatitis D virus (HDV) is the most severe form of chronic viral hepatitis. HDV is considered a satellite virus because it relies on hepatitis B surface antigen (HBsAg) to propagate. Currently, there is no approved FDA therapy for HDV in the USA. The recent LIMT-1 study demonstrated the safety and efficacy of Peginterferon Lambda (Lambda) monotherapy for chronic HDV (Hepatology.2023;77(6):2093-2103). Here we sought to predict Lambda mechanisms of action and efficacy using mathematical modeling of measured HDV RNA, HBsAg and alanine aminotransferase (ALT, which is a surrogate marker of infected liver cells (hepatocytes) death) kinetics.

I will present our efforts to characterize and mathematically model the unique frequent kinetic data of 33 chronic HDV-infected patients participated in the LIMT-1 study of Lambda 120 µg (n=19) or 180 µg (n=14), administered once weekly by subcutaneous injection for 48 weeks, with 24 weeks of follow-up. I will show how a mathematical model that includes hepatocyte proliferation can describe simultaneously HDV, ALT, and HBsAg kinetics using a nonlinear mixed-effects modeling approach. This study provides, for the first time, a comprehensive dynamic description of HDV response under Lambda monotherapy, estimate viral-host parameters and predict Lambda modes of action. Modeling suggests that Lambda blocks HDV viral production and mediates an increase in the death of HDV-infected cells that requires further study.