THU-364

Modeling suggests that undetectable HCV at week 2 of DAA therapy could identify patients for shorter treatment duration

Ashish Goyal¹, Ohad Etzion², Kimberly Page³, Tatyana Kushner⁴, Yedidya Saiman⁵, Scott Cotler¹, Harel Dahari¹

¹Program for Experimental & Theoretical Modeling, Division of Hepatology, Department of Medicine, Stritch School of Medicine, Loyola University Chicago, Maywood, IL, United States, ²Soroka University Medical Center, Beersheva, Israel, ³Division of Epidemiology, Biostatistics and Preventive Medicine, Department of Internal Medicine, University of New Mexico Health Sciences Center, Albuquerque, NM, United States, ⁴Division of Liver Diseases, Icahn School of Medicine at Mount Sinai, New York, NY, United States, ⁵Department of Medicine, Section of Hepatology, Lewis Katz School of Medicine at Temple University, Temple University Hospital, Philadelphia, PA, United States

Email: harel.dahari@gmail.com

Background and Aims:

The World Health Organization (WHO) calls for identifying predictors of successful treatment with reduced duration of DAA therapy. This objective is particularly important in people who inject drugs (PWID), in whom shorter treatment could improve adherence, decrease loss to follow-up, and reduce cost. In addition, there is a need to minimize DAA duration to reduce DAA exposure and increase acceptance in pregnant women. Here we investigate the feasibility of response-guided therapy (RGT) to reduce length of treatment using a computational modeling approach.

Method:

Previous modeling efforts based on ~300 patients receiving DAA (such as sofosbuvir + velpatasvir, elbasvir+ grazoprevir, sofosbuvir + ledipasvir, or pibrentasvir + glecaprevir) allowed us to characterize viral-host parameters, DAA efficacy in blocking HCV production, and treatment outcomes [Math Biosci. 2022 Jan;343:108756]. Based on this real-life patient data, parameter distributions were identified and then 20,000 parameter combinations of viral-host and treatment parameters were generated, each representing an in silico patient. Next, viral kinetic profile under DAA treatment for each patient was simulated using a multiscale model [Proc Natl Acad Sci U S A. 2013 Mar 5;110(10):3991-6]. The time to cure (TTC) for each in silico patient, defined as the time to reach less than one HCV viral copy in the 15L of extracellular body fluid, i.e. $V = 7 \times 10^{-5} \text{IU/ml}$ [Sci Rep. 2020 Oct 20;10(1):17820], was then estimated using mathematical modeling simulations.

Results:

Out of 20,000 in silico patients, about 10,000 (~50%) achieved undetectable HCV (<1 IU/ml) by day 14 after initiation of treatment. Modeling suggests that if HCV is undetectable on or before day 14 of DAA therapy, 90% and 98% of HCV-infected individuals can be cured within 4 and 5 weeks of DAA treatment, respectively. The median predicted TTC was ~22 days with ~0.6% reaching TTC as early as 2 weeks. Approximately 8% of these cases also had undetectable viral load at day 7, predicting that 90% and 98% cure rates could be achieved with 3 and 4 weeks of DAA treatment, respectively.

Conclusion:

Mathematical modeling of in silico patients that reach undetectable HCV by day 14 predicted that >90% cure rates could be achieved with 4-5 weeks of DAA therapy. This RGT could improve treatment access, facilitate HCV elimination, and reduce cost, particularly in patient groups most affected by HCV such as PWID.