Modeling of immune response suppression by hepatitis C virus and nivolumab treatment in chronic hepatitis C patients using quantitative systems pharmacology approach

Oleg Demin Jr

1Institute for Systems Biology Moscow

Objectives: To describe suppression of immune response by hepatitis C virus (HCV) and treatment of chronic hepatitis C patients with PD-1 inhibitor nivolumab.

Methods: Model describing chronic hepatitis C progression including HCV dynamics, fibrosis, ALT level, immune response suppression by HCV. The effect of HCV on immune cells was implemented as dependence of immune cell mediated death of infected hepatocytes on HCV level in blood. Nivolumab effect was described as increase in death of hepatocytes (both infected and normal) in accordance with mechanism of action of PD-1 inhibitors. The progression of chronic hepatitis C was calibrated against data on HCV, ALT, fibrosis score dynamics etc. The parameters of nivolumab effect was calibrated against data on HCV decline during therapy.

Results: Immune response suppression by HCV was calibrated against data on immune cell (CD8 and CD4 T cells, myeloid-derived suppressor cells) dynamics during treatment of chronic hepatitis C patients with PEG-interferon/ribavirin therapy. The model successfully describes the dynamics of HCV during treatment with nivolumab as well as response of different patients at follow-up. It was shown that the effect of nivolumab should be very strong to completely eliminate the HCV and infected hepatocytes.

Conclusions: Despite only very small part of patients are completely cured after nivolumab treatment, PD-1 inhibitors could be used in combination with direct antiviral agents to decrease the treatment duration and increase the percent of responders. Immunotherapy (including PD-1 inhibitors) is one of possible options to treat patients with chronic hepatitis C.