

Hepatitis C therapy: now more than a coin toss to achieve the cure

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The infection by the hepatitis C virus (HCV) remains a major public health problem worldwide, with about 170 million people chronically infected, 3 to 4 million new cases and more than 350 thousands of deaths each year (1). The scientific effort to improve the effectiveness of the treatment gradually increased the chance of cure for chronic hepatitis C (mainly for genotype 1, the most prevalent virus in the Western Hemisphere), which was increased from only 8% when interferon- α started to be used in the 1980s, to almost 50% using pegylated-interferon plus ribavirin, the most up-to-date therapy used in recent years. Nevertheless, the success rate was no better than that of the outcome of a coin toss, and a large number of patients that did not achieved sustained virological response (SVR, effectively representing a cure) is found in clinics with no effective treatment option.

In view of this critical situation, a new class of drugs was created, the HCV protease inhibitors, and in 2011 two molecules were approved for clinical use: boceprevir and telaprevir. These drugs interfere with the HCV replication ability by inhibiting the viral enzyme NS3/4A serine protease, and only work for HCV genotype 1 (2). It is the beginning of a new era in the hepatitis C treatment: the direct-acting antiviral (DAA) therapy.

Both molecules, in the phase 3 studies, had pegylated-interferon plus ribavirin as backbone,

adding the new drug to the standard therapy. For naïve patients, boceprevir increased the rate of success from 38% to 63-66%, and telaprevir from 44% to 69-75% (3, 4). Additionally, the results were more encouraging for those that needed the most, the unsuccessful therapy group. In previously treated patients, boceprevir augmented SVR from 21% to 66%, and telaprevir from 17% from 64% (5-7). These studies used pegylated-interferon plus ribavirin as control group, but the trials and the populations were not the same, so the results could not reflect the difference between the drugs.

These are better days, but new challenges come fast. The DAA therapy increased the adverse effects related to the standard therapy, mainly anemia with boceprevir, and rash with telaprevir. The emergence of resistance mutations and, consequently, treatment failure are a real threat as we learned with HIV therapy. High technology drugs are extremely expensive, so how to render them accessible to patients that require such therapy? Moreover, almost one third of the patients still will not be able to achieve SVR, how do we deal with this group? Again, history repeats itself: preliminary results of new DAA drugs plus standard therapy showed 90% of SVR in null-response patients (8). Place your bets!

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CONFLICTS OF INTEREST

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