

## A Key to Understanding Treatment Response in Hepatitis C

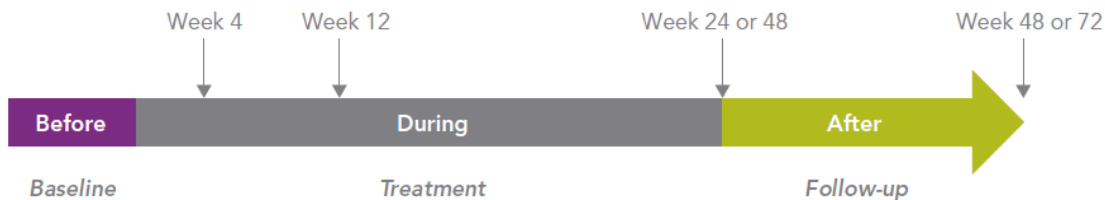
Hepatitis C is a liver disease caused by infection with the hepatitis C virus (HCV). Unlike other chronic infectious diseases such as HIV/AIDS, people with hepatitis C can be cured of the virus.<sup>1</sup> This means that drug therapy can remove hepatitis C from a person's blood so that it cannot be detected even when using very sensitive tests. Sustained virological response, or SVR – also known as viral cure – occurs when a person's hepatitis C remains undetectable six months after treatment ends.<sup>1</sup> Achieving a viral cure is important because it may reduce the risk a person has of developing liver failure and liver cancer, as well as other problems related to hepatitis C.<sup>2</sup>

Viral cure is the ultimate goal of hepatitis C therapy. Less than half of people with the most common type of chronic hepatitis C in the United States (genotype 1) achieve this goal with current treatments, which are given for at least 48 weeks.<sup>3,4</sup> The rate of viral cure is even lower for some groups of people, including Hispanics and African-Americans.<sup>5,6</sup>

This backgrounder provides a key to understanding response – and failure to respond – in people who are treated for chronic hepatitis C.

### How is treatment response measured?

Progress toward the goal of viral cure is assessed by measuring the amount of hepatitis C virus in a person's blood (also called HCV RNA or viral load) at specific times before, during and after treatment (Figure 1).



**Figure 1. Treatment response milestones.** A person's viral load is measured before treatment begins (at baseline) and at several key time points after treatment begins, including week 4, week 12, at the end of treatment (week 24 or 48), and 24 weeks after the end of treatment (week 48 or 72).

Important treatment response terms include:

- **Baseline viral load:** Amount of hepatitis C virus (HCV RNA) in the blood before treatment starts.<sup>1</sup> High baseline viral load means that the virus is reproducing rapidly and viral cure/SVR may be less likely to occur.<sup>4</sup>
- **Rapid virological response (RVR):** HCV RNA is not detectable in the blood at week 4 of treatment<sup>1</sup>; predicts a high likelihood of achieving viral cure/SVR.<sup>7</sup>
- **Early virological response (EVR):** HCV RNA cannot be detected in the blood at week 12 of treatment (complete EVR); or HCV RNA drops by more than 2 logs (100 times) from the baseline level by week 12 (partial EVR).<sup>1</sup> Not reaching EVR predicts a low likelihood of achieving viral cure.<sup>7,8</sup>
- **End of treatment response (ETR):** HCV RNA is not detected in the blood at the end of treatment.<sup>1</sup> For people with genotype 1 hepatitis C, the treatment period is typically 48 weeks with current therapies.<sup>1</sup>
- **SVR:** HCV RNA is not detected six months after treatment ends.<sup>1</sup>

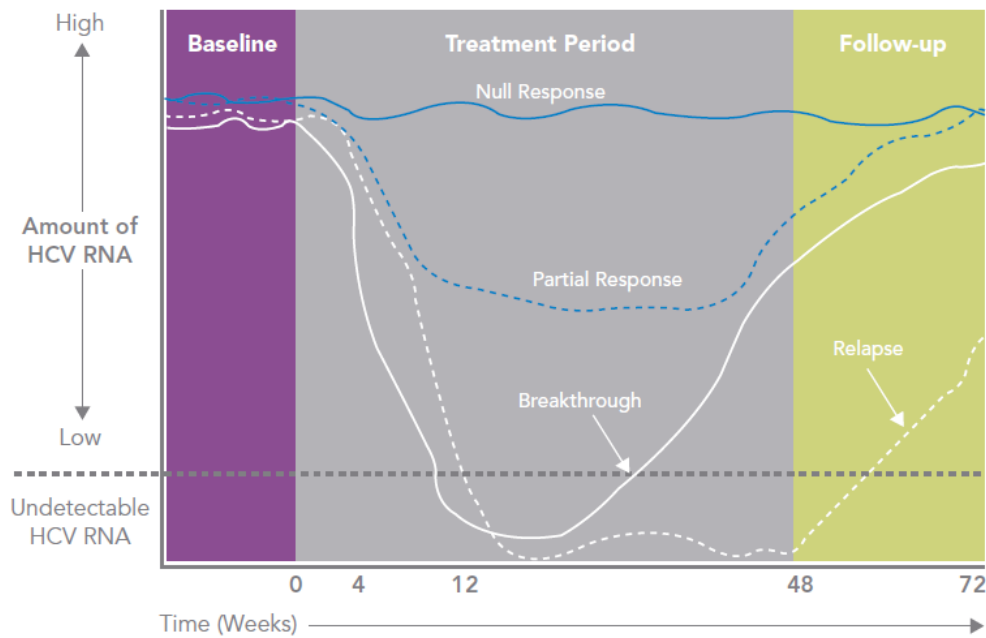
### What Is a Log?

Changes in hepatitis C viral load are measured in “log reductions.” Each log corresponds to a factor of 10. A 1-log reduction means that the starting (baseline) viral load dropped by 10 times; a 2-log reduction equals a 100-times drop; a 3-log reduction equals a 1,000-times drop; and so forth.

Measuring early response has become an increasingly important part of treatment for people with hepatitis C. For example, current guidelines recommend considering a shorter length of treatment for previously untreated people with genotype 1 hepatitis C who achieve RVR (24 weeks instead of the standard 48 weeks).<sup>1</sup> Additional early response measurements, such as undetectable virus at both week 4 and week 12 (also called “extended RVR”), are also being studied as ways to predict viral cure and decide on length of treatment.

### Failure to achieve a viral cure

Two main groups of people receive treatment for hepatitis C: 1) those who have not been treated before (treatment-naïve); and 2) those who have been treated before but have not achieved a viral cure (treatment-failure or treatment-experienced). Within the second group, failure to achieve a viral cure is described in various ways based on how a person responded to their previous therapy, as shown in Figure 2.



Adapted from Ghany MG, et al.<sup>1</sup>

**Figure 2. Failure to achieve a viral cure.** This chart shows four possible “pathways” for people who fail to achieve a viral cure:<sup>1</sup>

- **Null response (solid blue line):** Failure to reduce HCV RNA by at least 2  $\log_{10}$  (100 times) after 12 weeks of prior treatment, which is the currently recommended Food and Drug Administration (FDA) definition for clinical trials of investigational hepatitis C treatments.<sup>9</sup>
- **Partial response (dashed blue line):** At least a 2- $\log_{10}$  (100-times) drop in HCV RNA, but inability to fully remove the virus from the blood by week 24.
- **Breakthrough (solid white line):** After dropping to undetectable levels, HCV RNA is detected again in blood during treatment.
- **Relapse (dashed white line):** After dropping to undetectable levels, HCV RNA is detected again in blood after treatment ends.

People who don’t achieve a viral cure following their initial treatment course can later choose to try therapy again with current treatments (retreatment). However, only one in five people overall achieve a viral cure after retreatment, and the rate of success is even lower for people who never reach undetectable levels of virus during their initial treatment (null responders and partial responders).<sup>10,11,12,13</sup> People who fail to attain a viral cure remain at risk for serious liver damage.



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