

# ADVANCES IN HEPATOLOGY

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

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## Minimal Monitoring of Treatment for Hepatitis C Virus Infection



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### **G&H** What are the current recommendations for monitoring treatment for hepatitis C virus infection?

**MS** Two monitoring approaches are described in the American Association for the Study of Liver Diseases/ Infectious Diseases Society of America (AASLD/IDSA) guidelines, and European guidelines have similar recommendations. The traditional monitoring approach includes extensive pretreatment evaluation, on-treatment monitoring of laboratory testing, office visits, and monitoring after treatment to confirm sustained virologic response (SVR) or cure. In late 2019, the AASLD/IDSA guidelines panel released a simplified algorithm designed to pare down the tests needed before treatment and allow for minimal, if any, monitoring during treatment, in addition to checking for cure afterward. This monitoring approach targeted patients infected with hepatitis C virus (HCV) who were seen as uncomplicated or easy to treat, and focused on the pangenotypic treatment regimens of sofosbuvir/velpatasvir (Epclusa, Gilead) and glecaprevir/pibrentasvir (Mavyret, AbbVie), which are given for 12 and 8 weeks, respectively. The guidelines panel laid out specific criteria for each monitoring approach and separated patients into 2 groups, depending on whether they had cirrhosis. Most patients without cirrhosis could be treated by obtaining simple measurements such as a complete blood count and chemistry profile, determining the liver disease stage using an easily calculated scoring

system (eg, the Fibrosis-4 [FIB-4] score), measuring the virus level but not the genotype, and identifying factors for which patients should be excluded from minimal monitoring. One example is active hepatitis B virus infection, which is defined as being hepatitis B surface antigen (HBsAg)-positive. Patients who have been treated previously but failed to achieve cure should probably also be excluded from minimal monitoring, as these patients likely require an intensive approach to understand why treatment failed and to make sure that the second or third course of treatment is successful. Other HCV-infected groups that should be excluded from minimal monitoring include patients also infected with HIV (although I think this group is relatively simple to treat after accounting for drug interactions), women who are pregnant, liver transplant recipients, and patients who also have hepatocellular carcinoma.

It should be noted that patients with HCV infection who have cirrhosis have a separate simplified monitoring algorithm, but it requires more evaluation because cirrhosis is a serious medical condition that increases the risk of liver cancer as well as liver decompensation.

### **G&H** What have studies found regarding minimal monitoring of HCV treatment?

**MS** Several studies have examined this approach in a formal manner. First was an open-label, randomized, noninferiority trial conducted by Dr Gregory J. Dore

and colleagues, the results of which were published last year. Three hundred eighty patients infected with HCV who had never been treated and did not have cirrhosis were randomized to 8 weeks of glecaprevir/pibrentasvir treatment with simplified/minimal monitoring or standard monitoring (including visits essentially every 4 weeks). The study showed that treatment was quite safe and effective in both treatment arms. There was a slightly lower SVR rate in the simplified/minimal monitoring group compared with the standard monitoring group in the intention-to-treat population; however, in the per-protocol population, the SVR rates were 97% and 98%, respectively. These results demonstrated that minimal monitoring could achieve an SVR rate very close to that of standard monitoring with an identical safety profile.

ACTG5360, or the MINMON study, was also conducted on minimal monitoring of HCV treatment, and the results were presented first at last year's AASLD meeting and then were updated at this year's Conference on Retroviruses and Opportunistic Infections. I was one of the vice chairs of the study, and the chair was my Johns Hopkins colleague Dr Sunil Solomon. This study, which used the 12-week, single-tablet treatment regimen of sofosbuvir/velpatasvir, did not have a control group because HCV treatment is known to be highly effective in real-world cohorts. There was no baseline genotyping; patients were evaluated with HCV RNA, HBsAg, and the laboratory tests needed to calculate the FIB-4 score, namely a complete blood count and chemistry panel. Patients were given all 84 tablets of sofosbuvir/velpatasvir and did not have any follow-up office visits; they just received a telephone call or text message at 4 weeks to check how they were doing and then at 22 weeks after starting treatment to remind them to come in for a visit to test for cure (SVR). The study was performed in multiple countries, including Uganda, South Africa, Brazil, Thailand, and the United States, with more than two-thirds of the patients coming from outside of the United States. Overall, 95% of the patients were cured, which is very similar to what has been seen in registration trials and real-world data, where SVR has exceeded 95%, with minimal side effects and minimal dropout. This study underscores the reality that the medications to treat HCV infection around the world are relatively inexpensive because of generic manufacturing, and it is the laboratory testing, including genotyping, that makes HCV treatment prohibitive. The study shows that most patients without cirrhosis can be treated without the expense of additional testing or medical professionals to monitor them. Thus, to achieve the worldwide goal of HCV elimination, which requires the treatment of as many people as possible, there is no need for specialist health care providers; rather, patients need to be empowered by being given access to treatment

and being allowed to take the medication on their own without being monitored.

### **G&H** Are there any other advantages to using a minimal monitoring approach?

**MS** With the traditional treatment algorithm, patients must come into the office and undergo laboratory testing every 4 weeks. From a patient perspective, that requires quite a commitment. Patients have to stop what they are doing (whether it is work or other activities), come into the office, park a vehicle or arrange transportation, spend time waiting, see the provider, go to the laboratory for testing, and so on. Minimal monitoring removes those steps and makes it easier for patients to approach treatment. Treatment is no longer a commitment to come to the office and undergo frequent laboratory tests; it is just a commitment to taking pills every day for 8 or 12 weeks. If patients commit to taking medicine every day for the prescribed period of time, there is a 99% chance that they will be cured.

### **G&H** How has this approach been received by health care providers?

**MS** In my experience, most clinicians treating HCV infection have embraced the minimal monitoring approach. However, for some providers who have been treating HCV for more than a decade, it may be difficult to let go of what they remember of the challenges of interferon therapy. We need to drop these historical practices that do not improve treatment outcomes and need to reduce barriers to HCV cure.

Clinicians also need to move away from the concept of treatment-readiness and trying to decide when a patient is ready for treatment. All too often, there is a misconception about what it takes to be cured. The aforementioned studies have shown that giving patients without cirrhosis access to treatment can be quite successful, and many of those cured are patients whom providers were concerned would not adhere to therapy. Thus, clinicians should assume that patients are ready for treatment and move forward with treatment; this is a different mindset from the previous approach, in which patients needed to demonstrate readiness.

### **G&H** Is minimal monitoring becoming more widespread, particularly with the COVID-19 pandemic?

**MS** There is no question that the COVID-19 pandemic has forced the implementation of simplified monitoring. Many health care providers who treat HCV infection in

the United States switched to this approach during the pandemic. Patients could not come in for office visits, and providers wanted to avoid making patients go to the laboratory to limit any potential exposure to SARS-CoV-2. This minimal approach has been quite successful and has emerged as a more standard approach. I expect it to continue beyond the COVID-19 era.

### G&H What questions remain regarding patient selection for minimal monitoring?

**MS** Given the large number of patients treated and the known safety profiles of these therapies, providers should feel quite comfortable adopting a minimal monitoring approach. One question that remains, however, is which patients are good candidates for the minimal approach and which patients require a more comprehensive, holistic approach. For example, the opposite of minimal monitoring has been successful in patients with concurrent substance use disorder. In the ANCHOR study, the results of which were recently published in *Clinical Infectious Diseases*, patients received buprenorphine for opiate use disorder and, at the same time, sofosbuvir/velpatasvir for HCV infection. The study reported very good outcomes by treating the related conditions at the same time. Thus, although HCV infection can often be treated simply with minimal monitoring and minimal need for the expertise of specialists, it is important to treat the entire patient, and there may be patients with complex comorbidities for whom holistic care is needed. In the example of a patient with substance use disorder, focusing just on HCV treatment would miss the larger picture that the patient is at risk for overdose and other complications of substance use. Thus, treating both conditions makes more sense. There are also other examples in which treating the entire patient in a holistic manner makes sense. On the other hand, there are patients who do not have other conditions that need concurrent monitoring. Providers should simply give those patients access to treatment using a minimal monitoring approach.

### G&H What are the next steps in research for HCV management?

**MS** As mentioned, it is important to understand which patient groups require more holistic care. In addition, more work needs to be done on minimal monitoring approaches for people who inject drugs or people with

active substance use disorder for whom there is more concern regarding the risk of reinfection after treatment. It is important to understand which approaches are best and how therapy can be simplified while ensuring that providers are giving the appropriate comprehensive care that this group of patients needs. Another group that has been undertreated around the world, particularly the United States, is people in correctional settings. The advantages of a minimal monitoring approach for this group are obvious.

In addition, more research is needed to look at ways to bring treatment to patients. In medicine, particularly for HCV, there has been a practice pattern of making patients come to a doctor's office for treatment. This approach works well for symptomatic conditions. However, HCV is asymptomatic in most people. It is rarely an emergency, and asking people to travel distances to be treated will not always work. We need to work at taking minimal monitoring strategies and figure out how to further make treatment easy for patients. There are a number of projects underway looking at the rapid initiation of treatment in places such as methadone clinics, federally qualified health centers, or needle and syringe exchange programs.

### Disclosures

*Dr Sulkowski has served as a consultant for, and received research funding from, Gilead and AbbVie.*

### Suggested Reading

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