Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/gi-insights/exploring-the-hepatitis-b-treatment-landscape/13761/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Exploring the Hepatitis B Treatment Landscape

Dr. Buch:
The hepatitis B treatment landscape can be challenging to navigate. What can we do to improve our approach?

Welcome to GI Insights on ReachMD. I'm your host, Dr. Peter Buch. Joining us today to explore therapeutic options for hepatitis B is Dr. Robert Wong. Dr. Wong is a clinical associate professor at Stanford University, and he's passionate about reducing barriers to hepatitis B elimination.

Welcome to the program, Dr. Wong.

Dr. Wong:
Thank you, Dr. Buch, for having me.

Dr. Buch:
It's a pleasure. Let's start with some background. Dr. Wong, what are the current guidelines for the treatment of hepatitis B? And what are the limitations?

Dr. Wong:
Thank you, Peter, for that question. I think it's very important to highlight how we approach treatment for chronic hepatitis B. It can be a little bit complicated. Currently, there are several guidelines available for evaluation and management of hepatitis B. In the U.S., we rely primarily on the American Association for the Study of Liver Disease, or AASLD, treatment guidelines, but it's important to note that in different regions of the world—in Europe, Asia-Pacific regions—each have their own specific guidelines, and these variety of guidelines that are available differ slightly in their approach. The approach primarily relies on assessment of the severity of liver disease, liver enzyme elevation, viral load, and together help dictate whether someone is "eligible" or "not eligible" for treatment. The main premise behind this is really trying to identify hepatitis B patients that have the highest risk of disease progression and development of liver cancer and, therefore, those that have the greatest potential benefit of antiviral therapy.

But as you were sort of alluding to in the second part of the question, it becomes quite complicated, and this complicated algorithm of evaluating liver enzymes, viral load, liver disease severity may inadvertently create different challenges and barriers for patients and providers to accurately assess who is eligible for treatment. Furthermore, there are limitations in these treatment guidelines. As our understanding about hepatitis B epidemiology has advanced over the years, more studies have come out to really show that current antiviral therapies are not only safe and effective, but certain populations where we previously thought were ineligible or had very low risk of cancer and disease progression may still benefit from current therapies available. Thus, there is an important need to reassess our approach for antiviral therapy in chronic hepatitis B.

Dr. Buch:
Thank you. If we focus on simplifying this therapy, what kind of impact would that have?

Dr. Wong:
That's a fascinating question, and that is something that has definitely been discussed more and more in the recent years. The concept of simplifying therapy, or some may say differently expanding treatment eligibility, has always been controversial.

But the concept of simplifying therapy has many benefits. By simplifying it and making it uniform across regions and across guidelines really can reduce barriers to assessing for treatment and, therefore, linking patients that need treatment earlier. The other potential benefit of simplifying therapy is it incorporates some of the more recent data that show certain patients that were thought to be ineligible

actually can benefit from therapy. These patients that previously and currently, according to guidelines, that are not eligible have shown to continue to have risk of disease progression and continue to have risk of developing liver cancer, so simplifying therapies, lowering thresholds and expanding treatment eligibility has important clinical implications to suppress hepatitis B viral load and really reduce long-term risk of disease progression and liver cancer, which is really what we are trying to achieve with antiviral therapy in chronic hepatitis B patients.

Dr. Buch:
You know, Dr. Wong, this brings to mind a simplified approach in the hepatitis C arena that was recently proposed for general medical doctors. Could you comment a little bit about that and how that parallels hepatitis B?

Dr. Wong:
Yeah. That's a great comparison. Hepatitis C has been a fantastic success, and part of that success is due to increased advocacy to improve screening, improve linkage to care, and as you alluded to, the really simplified approach of treating.

We're not quite there yet in hepatitis B. The natural history and epidemiology of hepatitis B has identified that there are certain stages of hepatitis B infection, especially early in the course, seen particularly in younger individuals where they may be in a so-called immune-tolerant phase. Now, immune-tolerant means that the virus is present, but it doesn't generate liver injury, so these are situations where you may have an elevated viral load but normal liver enzymes which suggest no significant liver injury. But again, there have been recent studies showing that even in these so-called immune-tolerant phases, because of the high viral load, over time it does contribute to higher risk of liver cancer and liver disease progression.

The other important concept to remember that distinguishes hepatitis B from hepatitis C, hepatitis B is a DNA virus, and it integrates into our host genome, and because of that, the virus itself is a procarcinogenic virus, so it makes it even more important to recognize, identify and initiate treatment early to suppress viral replication because that has been clearly shown to increase long-term risk of liver cancer. I do see in the future that we may get to the point where we are treating all patients with chronic, active hepatitis B similar to the approach that we are currently doing with chronic hepatitis C.

Dr. Buch:
Thank you. Let's talk about nucleotide therapy. What's the optimal duration for this therapy?

Dr. Wong:
Great question and a tricky answer. When someone starts antiviral therapy, what is the endpoint, at which point we think about stopping therapy? This is a moving target and a bit controversial but also very exciting. The ideal endpoint of therapy is eradication of virus, and, and this ideal outcome means you completely get rid of the integrated virus, which we call the cccDNA. These are the integrated aspect of the virus. In our current lifetime, most experts would say this is nearly impossible and out of reach. Therefore, the intermediate outcome that most clinical trials now are focusing on as an endpoint of therapy is what we call functional cure, and what that means is if you can eradicate surface antigen. So, surface antigen is what defines chronic hepatitis B. If you can transition a surface antigen from positive to negative, achieve undetectable viral loads and normalize ALT, those are the three core components of functional cure and if we can achieve that, that can be a potential, time period where one can discontinue therapy and monitor. That is also a tricky endpoint. With current therapies that we have available the proportion of patients achieving that are in the single digits per year.

Dr. Buch:
Thank you. For those just tuning in, you're listening to GI Insights on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Robert Wong about treating hepatitis B. So, Dr. Wong, let's explore alternative therapies to nucleotide therapy. How do interferons fit in?

Dr. Wong:
Great question. Interferons has always gotten a bad rap, especially during the hepatitis C era, but interferons actually is considered one of the first-line treatment options for chronic hepatitis B. It's not used often because of the side effects, which we know about from the hepatitis C era, but also because studies have shown that interferon is most effective in certain subtypes of chronic hepatitis B based on genotype, based on viral loads. And even in those highly selected populations, the success of achieving surface antigen loss or functional cure is still not very high. So, in the vast majority of individuals, interferons really do not play a major role in the current treatment approach..

Dr. Buch:
And if we move on to preventive care, how do you approach treatment for a hepatitis B vaccine nonresponder?

Dr. Wong:
Nonresponders to vaccination is not uncommon. The approach to this is really ensuring that patients got, the correct schedule of vaccinations. You can also check for quantitative levels of surface antibody. And if there is detectible levels or measurable levels of

antibody, then they do not need further boosters.

Dr. Buch:
And if we tease out the question a little bit further, what do we do for those patients with hepatitis B vaccine who do not develop antibodies despite two or three vaccinations?

Dr. Wong:
There's not strong evidence, but it is clinically reasonable to give an additional booster to see if that can, perhaps, stimulate immunogenicity.

Dr. Buch:
And that leads to the third question, because some of our colleagues out there may have colleagues in the healthcare field who have had these vaccinations who do not have antibodies. So, what are you going to recommend for our colleagues out there who are faced with this dilemma?

Dr. Wong:
Yeah. For those patients that continue not to have reactivity, it is reasonable to give an additional single-dose booster. After that I would not recommend further boosters and sort of clinical monitoring.

Dr. Buch:
Thank you. That's very helpful. And before we conclude, Dr. Wong, are there any final thoughts you'd like to share with our audience today?

Dr. Wong:
I think this has been such a fascinating discussion, and I think it's critically important to sort of emphasize, the novel improvements in treatments of hepatitis B. And I know we touched on vaccination, which is a very important preventative approach, but I would raise awareness and the importance of also thinking about screening. You know, despite the availability of hepatitis B tests, as a country but also globally, we still have a lot of work to do in improving screening for hepatitis B. Current screening approach is still risk-based, which is also complex, introduces potential patient stigma, and there is a movement—and I certainly support that movement—to expand hepatitis B screening to a universal approach. So I think when we think about hepatitis B, we really need to think about the entire cascade of care, screening effectively, linking those to care and ensuring adequate and timely assessment for treatment eligibility.

Dr. Buch:
With that important and informative information in mind, I want to thank my guest, Dr. Robert Wong, for sharing his insights on the treatment of hepatitis B. Dr. Wong, it was a pleasure having you on the program today.

Dr. Wong:
Thank you so much, an absolute pleasure as well.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit ReachMD.com/GIInsights where you can be Part of the Knowledge. Thanks for listening, and see you next time.