

HEPATITIS C VIRUS INFECTION, A SILENT PLAGUE OF THIS CENTURY. IS DISCOVERY OF SOFOSBUVIR A PARADIGM SHIFT ?

Being in practice of adult medicine for the past three decades and treating various patients with varied symptoms has always motivated me to continue finding new advances in better care. I can understand the amount of inconsistency in the awaited results faced by many physicians like me knowing the fact that in human body the two plus two never always results in four.

I received an e-mail on the weekend and I saw this all new concept of Oral Antivirals Cocktails to treat HCV infection just as we have loads of options for HBV infection. To add to flavor is the fact that the results at viral clearance will also be much better as would be side effect profile. I am dropping a few lines just to sensitize the readers regarding this all new drug Sofosbuvir, licensed this month with the name of Sovaldi manufactured in the US by Gilead Pharmaceuticals.

Ironically most people who are infected with HCV do not know it, because it can take decades for the virus to damage the liver sufficiently to cause symptoms.

Researchers and patients have been disappointed before, when the first two direct-acting antiviral pills, Telaprevir and Boceprevir, reached the market in 2011. The drugs, which inhibited the virus's protease enzyme along with Simipravir which has yet to get the approval of FDA have lost the race because of the need to be combined with Pegylated Interferon and Ribavirin. Nevertheless they raised the cure rate to about 70 percent. Have they played the role of being Game Changers as anticipated? Well I don't think so.

Sofosbuvir is an NS5B polymerase inhibitor and the first drug in this class to be reviewed in the US and FDA approved it on 6th December, 2013. It is intended to be administered as a 400-mg oral dose once daily in combination with other drugs. If I have to simplify the mechanism of action of Sofosbuvir omitting all the difficult medical jargon, I would say that it is an evil decoy of sorts. It looks like a building block of RNA. But once it is mistakenly incorporated into the RNA chain, the chain cannot grow and the virus cannot reproduce.

An advisory committee to the US FDA voted unanimously (15-0) to recommend Sofosbuvir (Gilead Sciences, Inc) in combination with Ribavirin for the treatment of adults with chronic hepatitis C virus (HCV) genotypes (GT) 2 and 3 infections, the most frequent genotypes in Pakistan.

The committee also recommended (15-0) Sofosbuvir in combination with Pegylated Interferon and Ribavirin for treatment of chronic HCV in treatment-naïve adults with GT 1 and 4 infections.

The Sofosbuvir approval is supported primarily by data from four phase 3 studies, NEUTRINO, FISSION, POSITRON and FUSION, in which 12 or 16 weeks of Sofosbuvir-based therapy was found to be superior or non-inferior to currently available treatment options or historical controls, based on the proportion of patients who had a sustained virologic response (HCV undetectable) 12 weeks after completing therapy (SVR12). Patients who achieve SVR12 are considered cured of HCV.

Hepatitis C is a slow-developing disease, so there's no immediate rush to treat newly diagnosed patients as witnessed by the drop off in sales in the US (42%) of Pegylated Interferon in 2013. Many doctors are now warehousing their hepatitis C patients, urging them to forgo treatment until the new drugs are approved. This was well expected as Sofosbuvir was able to draw the attention of all the practicing physicians and seeing the results in all the trials has further pushed them to counsel their HCV infected patients to wait. This new drug is likely to alter the calculus about who gets treated and when.

Sofosbuvir will cost \$1,000 per pill. A typical course of treatment will last 12 weeks and run \$84,000 in USA, plus the cost of necessary companion drugs. Some patients may need treatment for twice as long. Having said that the typical course of Pegylated Interferon along with Ribavirin costs around \$1,20,000 in USA. Those who are bold and go out and innovate molecules like this and take the risk — there needs to be a reward on that. Otherwise, it would be very difficult for people to make that investment. I maintain that the high price is fully justified. We have just to look at the value that this drug is bringing into the health care system and to the patients.

I found it interesting to share while going through the official website of Gilead that it plans to charge far less for a course of the drug in places such as India, Pakistan, Egypt and China, where most people with hepatitis C live. Pressed by many as to how low the price of a cure will go, Mr. Gregg Alton, the Company's Vice President is found saying: "I don't think we'll be able to get it into the low hundreds. But I think we can get it into an affordable range for them. It'll be from the high hundreds to low thousands for these types of markets."

Having said all this, I also carry this fear that it is just this type of promotion that gets people excited enough to not take the time to get the entire story. Fear and desperation go a long way to allow some catastrophic results from drugs and treatments released before ALL the facts are reported.

Cautiously pray this is all true, but proceed with caution, and be prepared to use some objectivity

before running headlong into these options. I also feel content knowing the fact that when this drug will reach my market a lot more will be known about it.

The general wisdom of the doctors treating their patients should prevail as always.

Critics and comments are always welcomed.

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