The REAL Drug to Beat in Hepatitis C Treatment: Ribavirin

A biopharma and pharmaceutical industry veteran shares his thoughts on the drug to beat in the hepatitis C drug development rush.

April 8, 2013 By Chris Barnes

By now, most of us are aware – some of us painfully so – that the Hepatitis C drug development market is red hot. Investors and developers alike need a scorecard to keep track of who is buying who and for what potential blockbuster drug in the race to make it big in treating Hepatitis C. All of this hullabaloo is for good reason – the CDC estimates there are over 170 million people infected with Hepatitis C worldwide[1], a vast majority of them don't know that they have it. That is paradoxically both an enormous and lucrative problem. This means there are a lot of potential patients for pharmaceutical companies to treat with blockbuster anti-HCV drugs.

The names of the compounds in development are like alphabet soup – GS-7977, VX-222, BMS-790052, BI-201335, TMC 435, BL-8020 protease inhibitors, polymerase inhibitors, cyclophilin inhibitors the list goes on and on. This is a good thing for both drug makers and patients. Drugs to treat Hepatitis C are becoming more potent and more tolerable. And the race for the next blockbuster drug means there is no shortage of drugs and drug classes to choose from. Drug developers may even realize the holy grail of Hepatitis C treatment – an all oral, interferon-free regimen consisting of 2-4 pills a day. That's right, no shots, no interferon. This would potentially make treatment for Hepatitis C infinitely more tolerable for patients.

So the HCV drug development biz is booming but the hottest drug to beat in Hepatitis C? Ribavirin. A cheap, generic anti-viral. It turns out that even with all the advances drug makers are realizing in interferon-free drug combinations, ribavirin is critical to the success in curing patients of Hepatitis C. The trouble is that no one is really sure how ribavirin works. All we know is that treatment response rates are infinitely higher when it is part of a Hepatitis C antiviral regimen.[2][3][4]

Researchers are busy trying to find out just what makes ribavirin tick, but let's look at a few of the current theories on how the drug works:

Ribavirin may cause something called 'error catastrophe' in the lifecycle of the HCV virus.[5] Ribavirin is a nucleoside analog – this means that ribavirin can fool the virus into thinking that it's

one of the building blocks needed for the virus to replicate. So when the virus tries to replicate itself, it picks ribavirin as a building block instead of the real thing. This mucks up the replication process leading to 'error catastrophe' – in other words, the virus is no longer able to make copies of itself.

Inosine monophosphate dehydrogenase (IMPDH). That's a tongue-twister to be sure, but it's also a cellular enzyme the human body makes and the HCV virus needs. Ribavirin may inhibit this enzyme, which consequently shuts down the energy supply the Hepatitis C virus requires to survive and replicate.[1] The Hepatitis C virus is sneaky. It has a peculiar knack for evading the body's immune system[2], so anything that might disrupt that ability would be very valuable to an anti-HCV regimen. It turns out that ribavirin may have this unique ability by helping the body mount a specific anti-viral response to the Hepatitis C virus, which is essential in fully clearing the virus.[3]

While ribavirin's exact mechanism of action remains a mystery, there is one thing we do know for certain – we need ribavirin to fight Hepatitis C. Paring ribavirin with the above new antiviral compounds currently in development – called Direct Acting Antivirals or DAAs - that target and disrupt numerous points in the lifecycle of the virus, lead to significantly better cure rates then just using the DAAs alone. While interferon may go the way of the buffalo, it appears that the lowly, unsexy ribavirin is here to stay. This makes ribavirin the REAL drug to beat in the Hepatitis C drug development marketplace.

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References

[1] Perz JF, et al. The contribution of hepatits B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. J Hepatol 2006; 45: 529-38

[2] Vertex Pharmaceuticals, Inc. (2010) Vertex adds ribavirin in additional treatment arm in ongoing phase II VX-222 & Telaprevir combo trial. [Press Release] Retrieved from http://viralmatters.blogspot.com/2010/11/vertex-adds-ribavirin-in-additional.html

[3] Hezode, Christopher, et al. (2009) Telaprevir and Peginterferon with or without Ribavirin for chronic HCV Infection. Retrieved from http://www.nejm.org/doi/full/10.1056/NEJMoa0807650

[4] Smith, M. (2012). New Combo KOs HCV Without Interferon, Ribavirin [Online article] Retrieved from: http://www.medpagetoday.com/InfectiousDisease/Hepatitis/30739

[5] Maag D, et al. RNA virus error catastrophe: direct molecular test by using ribavirin. Proc. Natl. Acad. Sck. 2001; 98: 6895-900