

Q & A with Karen Tashima, MD

New Direct-Acting Antiviral Agents Offer Therapeutic Revolution for Hepatitis C Virus Infection

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PROVIDENCE – Hope is here for the estimated 5.2 million persons¹ in the United States with chronic hepatitis C virus (HCV) infections. Twenty-five years after the identification of the virus through cloning techniques, revolutionary direct-acting antiviral agents (DAAs) offer the promise of a cure for a significant number of those affected.

Dr. Karen Tashima, Site Director of HIV Clinical Studies and Clinical Research Site Leader of the AIDS Clinical Trials Unit at The Miriam Hospital, is also a principal investigator in studies of these new DAA medications. In addition, she is engaged in follow-up studies with those patients whose virus been eradicated to make sure it is cured for the long-term; there are also two trials underway at Miriam for HIV-HCV co-infected patients.

Recently Dr. Tashima discussed these revolutionary therapeutic agents and the economic challenges they present.

Q. The mainstay of care to treat HCV infection has been interferon and ribavirin. Do the new direct-acting antivirals (DAAs) replace that?

A. There had been incremental advances in the treatment of HCV with interferon, such as giving injections in the pegylated form once a week, rather than injections three times a week. Then ribavirin came along and increased a patient's chance of cure. Cure rates were still pretty low, around 50 percent. But only 10-20 percent of patients with HCV infection could be cured if they also had HIV infection.

We've been waiting a long time for direct-acting agents. Interferon is poorly tolerated in many people, with side effects such as flu-like symptoms, often resulting in time loss from work. There are also contraindications in the use of interferon in patients with significant cardiac, pulmonary, and psychiatric diseases such as uncontrolled depression, or in poorly controlled diabetes.

Understanding how well these DAAs work, and if we still need to use pegylated interferon and ribavirin, is what we are investigating. Studies are underway testing different genotypes and different combinations of drugs. So, for example, in patients with genotypes 1-4, the FDA has approved the DAA Sovaldi (sofosbuvir) to be given with pegylated interferon and ribavirin for 12 weeks. For a sub-group of patients, the FDA approved sofosbuvir for genotype 1 and 4 patients even without interferon. For patients with genotypes (2 and 3), Sovaldi can be given with ribavirin alone for a high rate of cure.

Q. Are different DAAs combined in treatment protocols?

A. These are really targeted designer medications. The first one to be FDA-approved was Sovaldi (sofosbuvir) made by



Dr. Karen Tashima, Professor of Medicine in the Division of Infectious Diseases at Brown, stands by a painting in her office, a memento of her years as ID Fellowship Director, 2005-2012, presented to her by the Infectious Disease Fellows last year.

Gilead Sciences. We have a study going on now with Gilead combining different oral agents. We are also working with Bristol-Myers Squibb (BMS) on a drug called daclatasvir and combining that with other drugs. And Abbott has a three-drug regimen that we think will be approved by the FDA within this year.

Q. Can DAAs be used in people with hepatitis C-related liver cancer, advanced liver disease, or after liver transplant?

A. We're prioritizing the patients who have advanced liver disease, such as stage 3 or 4 fibrosis, and those who are most at risk for liver failure. Some of the DAAs, such as sofosbuvir, are safe in people with advanced liver disease, including decompensated cirrhosis, while awaiting liver transplant. If we cure the hepatitis C we might prevent liver cancer. The FDA approved sofosbuvir for use in patients with hepatitis C-induced liver cancer. If a patient needs a liver transplant, the DAAs are used to prevent hepatitis C from coming back in the newly transplanted liver.

Q. What are the prospects for the development of an HCV vaccine?

A. Currently there is no effective vaccine but researchers are investigating possible approaches.

Q. According to the Centers for Disease Control (CDC), more than 75% of adults infected with HCV are Baby Boomers, people born from 1945 through 1965. Why is the highest prevalence in this cohort?

A. Before hepatitis C was identified, the disease was called non-A, non-B hepatitis.

Non-A, non-B was transmitted through unsafe blood transfusions before widespread screening of the blood supply, through high-risk behaviors such as injection drug use, and there were transmissions in the healthcare settings back then, before widespread institution of universal precautions. With screening of the blood supply and safe infection control practices, we avoid HCV transmission in the healthcare setting.

Q. What should practicing physicians know about HCV?

A. It's a reflex for doctors to check for hepatitis A, B, C when they see elevated liver enzyme levels. But people can be fully asymptomatic for 20-40 years, and may even have normal liver-related blood tests. The only hint might be the appearance of cirrhosis. Knowing which patients should be tested is important. (See sidebar.) The hepatitis C antibody test is

the first you should do. If it comes back positive there is a specific RNA test for the virus to identify patients with chronic hepatitis C infection (as opposed to prior infection and clearance of the virus spontaneously or due to prior effective therapy).

Q. There has been controversy about the cost of these DAAs – as much as \$1,000 a pill. A combination of these agents could double or triple the price. What are your thoughts on this?

A. There are a lot of companies working on hepatitis C treatment, and with more competition hopefully the prices will

come down. It's very early on with the hepatitis C drugs and I think insurance companies will help pay for the cost. We are talking about three months of treatment and that's it. The downside of not treating HCV is expensive care for complications of liver failure, need for liver transplantation, or death.

Reference

1. Chak E, Talal AH, Sherman KE, Schiff ER, Saab S. Hepatitis C virus infection in USA: an estimate of true prevalence. *Liver Int.* 2011 Sep;31(8):1090-101.

FIND OUT IF YOU HAVE HEPATITIS C
IT COULD SAVE YOUR LIFE

BORN FROM 1945-1965? SOME PEOPLE DON'T KNOW HOW OR WHEN THEY WERE INFECTED

People born from 1945-1965 are **5X MORE LIKELY TO BE INFECTED WITH HEPATITIS C**

3 OUT OF EVERY 4 people with Hepatitis C were born between these years

Up to **75%** of people living with Hepatitis C **DO NOT KNOW THEY ARE INFECTED**

Many people can live with **HEPATITIS C** for **DECADES** WITH **NO SYMPTOMS**

HEP C Blood Test CDC recommends anyone born from 1945-1965 **GET TESTED**

TESTED	NOT TESTED
KNOWING YOU HAVE HEPATITIS C can help you make important decisions about your health	LEFT UNTREATED, HEPATITIS C can cause liver damage and LIVER FAILURE
Many people can get LIFESAVING CARE AND TREATMENT	HEPATITIS C is the #1 CAUSE OF LIVER TRANSPLANTS
Successful treatments can ELIMINATE THE VIRUS from the body	HEPATITIS C is a leading cause of LIVER CANCER

Don't go down the wrong path, talk to your doctor about getting tested. It could save your life.

CDC U.S. Department of Health and Human Services Centers for Disease Control and Prevention **KNOW MORE HEPATITIS**

WHO SHOULD BE TESTED?

Routine testing of asymptomatic persons:

Persons who should be tested once for hepatitis C virus (HCV) infection without prior ascertainment of HCV risk factors include:

- People born during 1945 through 1965

Persons who should be tested routinely for hepatitis C virus (HCV) infection based on their risk for infection include those who:

Currently inject drugs

Ever injected drugs, including those who injected once many years ago

Have certain medical conditions, including persons:

- who received clotting factor concentrates produced before 1987
- who were ever on long-term hemodialysis
- with persistently elevated alanine aminotransferase levels (ALT)
- infected with HIV

Were prior recipients of transfusions or organ transplants, including persons who:

- were notified that they received blood from a donor who later tested positive for HCV infection
- received a transfusion of blood, blood components or an organ transplant before July 1992

Persons who should be tested routinely for HCV-infection based on a recognized exposure:

- Healthcare, emergency medical, and public safety workers after needle sticks, sharps, or mucosal exposures to HCV-infected blood
- Persons who have received medical or dental interventions in health care settings where infection control practices are substandard
- Persons who have received blood in countries where serological testing of blood donations for HCV is not routinely performed
- Persons who have had tattoos, body piercing or scarification procedures done where infection control practices are substandard
- Children born to mothers infected with HCV
- Persons who have used intranasal drugs
- Prisoners and previously incarcerated persons

(Source: CDC) <http://www.cdc.gov/hepatitis/HCV/GuidelinesC.htm>