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United States to approve potent oral drugs for hepatitis C

Improved treatments offer hope for eradication of viral liver infection.

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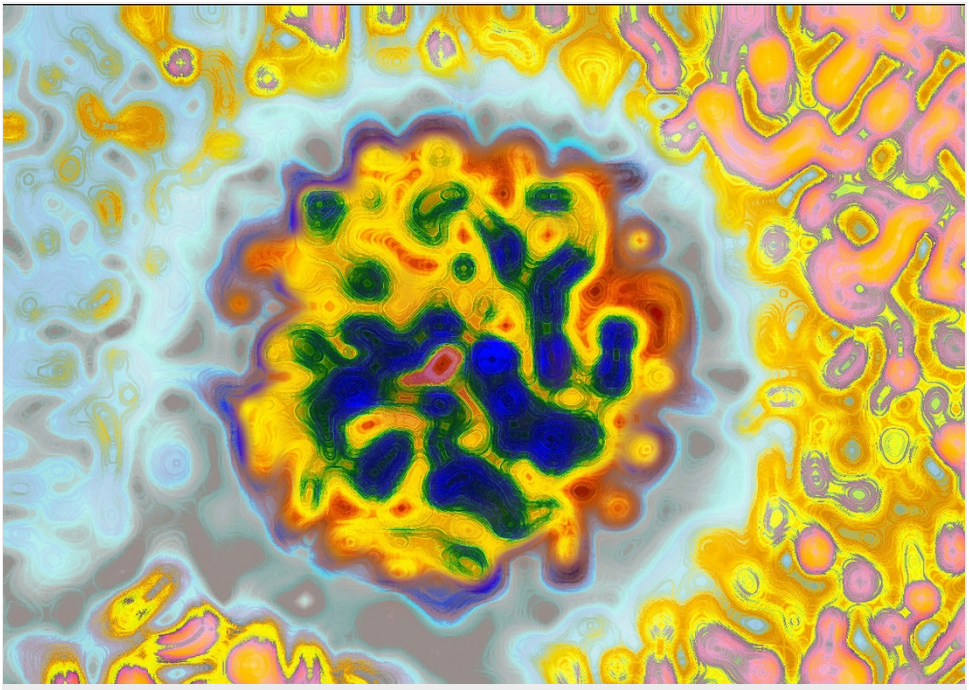

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Cocktails of new oral antiviral drugs to fight hepatitis C have aced clinical trials.

For decades, people with hepatitis C virus (HCV) have had to endure gruelling treatment regimens that include injections of the drug interferon, which can cause severe nausea and depression. But with the imminent approval of several highly effective oral antiviral drugs, and more on the way, researchers say that eradicating the infection worldwide is now a realistic goal.

Unlike previous HCV treatments, which sought to enhance the immune system with interferon and other drugs, the latest group of oral medications interferes with the virus's ability to replicate and make proteins. A US Food and Drug Administration (FDA) board recommended two such drugs — simeprevir, made by Johnson & Johnson in New Brunswick, New Jersey, and sofosbuvir from Gilead Sciences in Foster City, California — for approval last week. When each is taken in combination with a drug called ribavirin, the treatment eliminates hepatitis C in around 80% of people.

"This is the first time in the history of humankind that we have a cure for a viral disease," says pharmacologist Raymond Schinazi of Emory University in Atlanta, Georgia.

Findings from trials of different drug combinations are set to be released this week. A phase II study called COSMOS tested a combination of sofosbuvir and simeprevir in 197 people with HCV who had either not responded to interferon or who had advanced liver fibrosis caused by the virus. After 12 weeks of treatment, the drugs completely cleared the virus in more than 90% of participants.

Another study, led by physician Kazuaki Chayama at Hiroshima University in Japan, treated 220 people with a combination of daclatasvir and asunaprevir, two new drugs from Bristol-Myers Squibb in New York. The cocktail cured 85% of participants. Eric Hughes, lead global medical researcher at the company, says that it plans to submit the drugs for FDA approval in 2014.

Stopped short

Despite such encouraging results, larger studies of drug combinations involving multiple drug companies seem to be unlikely. Charlotte Edenius, vice-president of development at Medivir, a drug company in Stockholm that collaborated with Johnson & Johnson on the COSMOS study, says that Gilead and Johnson & Johnson do not plan to work together for a phase III trial. Similarly, a Bristol-Myers

Squibb spokesperson says the company has no plans to collaborate with Gilead on larger trials of a combined sofosbuvir–daclatasvir therapy, despite a phase II trial completed earlier this year in which the drug pairing cured all 41 participants.

Even without phase III trials or FDA approval for this approach, David Thomas, a hepatitis C researcher at Johns Hopkins University in Baltimore, Maryland, expects that some physicians will begin prescribing such combinations 'off-label' for difficult-to-treat cases.

And, he says, the impressive cure rates achieved in clinical trials suggest that potent drug combinations could eradicate HCV worldwide — at least in theory. The virus does not have an animal reservoir, meaning that it is not harboured by other animals, and it is not easily spread between people, except through blood. Improved screening of blood supplies used for transfusions and better patient-screening techniques have already greatly cut transmission rates over the last 15 years. Emergence of drug-resistant virus strains could be a hurdle, adds Thomas, but they might be rare because the latest antiviral drugs are so potent in combination.

Price problem

Hepatologist Rajender Reddy at the University of Pennsylvania in Philadelphia sees a second stumbling block: getting such treatments to people who need them. Many of the roughly 170 million people worldwide who carry hepatitis C will not be able to afford the drugs, he says. There is also little incentive for drug companies to lower costs — unlike antiviral therapies for HIV, which must be taken for a patient's lifetime, HCV treatment is given for only 12 weeks.

Identifying HCV carriers is also challenging, because most people do not know that they have the disease until they develop severe cirrhosis or liver cancer — sometimes decades after being infected. Mandatory screening of at-risk populations such as the elderly and drug users would need to be a major part of an eradication effort, says virologist Charles Rice of Rockefeller University in New York. Crucial too is education to prevent people from contracting the disease in the first place. Even the most effective oral drugs do not raise a lasting immune response against the virus, and people can be reinfected.

That is why the search for a preventative HCV vaccine continues, with the most promising ones currently in phase II clinical trials. “Even if we have all the drugs we need — which is still an open question — it will be decades, if not a century, before it’s gone,” says Rice.

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