



Seeking a lasting cure for hepatitis B

For millions of people living with chronic hepatitis B, long term treatment has been the only option. EU funded researchers are joining forces to develop combination therapy that could one day free patients from lifelong medication.

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Hepatitis B is a chronic infection affecting roughly 254 million people worldwide and causing about 1.1 million deaths each year, mainly from cirrhosis and liver cancer. Although a preventive vaccine has been available for more than 40 years, there is still no cure for people already living with the disease. Current antiviral medicines can suppress the virus, but cannot eliminate it.

According to the [European Centre for Disease Prevention and Control \(ECDC\)](#), around 3.6 million people in the 27 EU countries, Iceland, Liechtenstein and Norway are chronically infected with hepatitis B. Many do not realise they are infected until serious liver damage has already occurred, leaving them on lifelong treatment.

“People think we have solved the problem because we have a preventive vaccine. But for the millions already living with chronic hepatitis B, that is simply not true,” said Professor Ulrike Protzer, director of the Institute of Virology at the Technical University of Munich and Helmholtz Munich.

Now, however, Protzer and other researchers across Europe believe a functional cure may finally be within reach.

Protzer has spent more than two decades studying how hepatitis B evades the immune system, and developing new ways to help the body fight back.

“I call hepatitis B the most frequent neglected disease in the world,” said Protzer, who is leading an international team of researchers developing a new vaccine for people living with chronic hepatitis B.

Their work is part of the six-year EU-funded TherVacB research initiative that concludes at the end of 2026. While conventional hepatitis B vaccines prevent infection, this therapeutic vaccine is intended for people who are already chronically infected.

Rather than trying to attack the virus directly, Protzer’s team is asking a different question: can the immune system itself be trained to regain control? The aim is to recreate the type of immune response seen in people

who naturally clear hepatitis B after becoming infected later in life.

“People who eliminate the virus develop strong antibody and T-cell responses,” said Protzer, referring to immune cells that detect and kill infected cells. “We designed our therapeutic vaccine to activate exactly those kinds of immune responses.”

Early clinical studies in healthy volunteers showed the vaccine was well tolerated and successfully stimulated the expected immune response. Patient trials are now underway in Germany, Italy, Spain, the UK and Tanzania.

While the researchers caution that the work remains in its early clinical stages, they believe therapeutic vaccines could eventually become an important component of future combination treatments.

Cause for hope

The World Health Organization aims to eliminate viral hepatitis as a public health threat by 2030. Achieving that goal will require earlier diagnosis, wider vaccination and more effective treatments for people already living with chronic infection.

Growing optimism in recent years comes from a shift in scientific thinking. Rather than relying on a single treatment to eliminate the virus, researchers increasingly believe that a functional cure will come from combining therapies that work effectively together, allowing patients to keep the virus under control without continuous treatment.

“We are entering a very exciting time in hepatitis B research,” said Dr Maria Butí Ferret, a hepatologist with decades of experience treating patients with the disease.

“Many new treatments are being developed, targeting different parts of the virus or helping the immune system fight it more effectively. The future will probably not come from a single treatment, but from combining different approaches that work together.”

Butí Ferret is a professor of medicine at the Universitat Autònoma de Barcelona and a senior hepatologist at Hospital Universitari Vall d’Hebron, one of Europe’s leading liver disease centres.

For the past six years, she has been part of another international research team supported by the EU called IP-cure-B, which investigates whether scientists can restore the immune system’s ability to control hepatitis B naturally.

Current antiviral medicines cannot remove the tiny viral reservoir that remains hidden inside liver cells. As soon as treatment stops, the virus often returns.

Researchers in IP-cure-B therefore explored whether they could “wake up” the body’s own defences before stopping antiviral medicine. In this way, the immune system would be better prepared to keep the virus under control in the long term.

The project’s Phase IIa clinical trial has now been completed, with researchers analysing whether this immune-based approach can achieve a functional cure. Alongside the clinical trial, the team is also searching for biological clues in patients’ blood and immune systems that could reveal who is most likely to benefit from future immune-based treatments.

“What we learn won’t only be relevant for our own study,” said project coordinator Fabien Zoulim, professor of medicine at Claude Bernard University Lyon 1, France, and one of Europe’s leading experts on chronic hepatitis B.

“It could also help us understand which patients are most likely to respond to the new immune-based treatments or direct acting antivirals that are now emerging.”

Combining strengths

Increasingly, scientists think that combination therapy will be the key. If the virus is first reduced using antiviral medicines or new antiviral technologies, the immune system may then be better able to respond to therapeutic vaccines or other immune-based treatments.

Recognising that no single approach is likely to solve the problem alone, the TherVacB and IP-cure-B teams teamed up in 2023. They shared expertise and compared findings as they explored how different immune-based strategies could ultimately be combined to improve patients' chances of achieving long-lasting relief.

"If virus levels remain high, immune cells become overwhelmed," Protzer explained. "The logical approach is first to reduce the amount of virus and then activate the immune response."

Zoulim believes these new approaches will also make treatment more personalised. "The objective is to better characterise patients and propose the best treatment according to their own specific situation," he said. "Precision medicine for hepatitis B will be a must to optimise the hepatitis B virus cure rates."

Promise of a cure

Recent clinical advances have strengthened that optimism. Several experimental therapies have shown that a functional cure is achievable in a proportion of patients, transforming expectations for a disease once considered incurable.

"Living with a chronic infection is not only a medical issue, it can also have an emotional and social impact," Butí Ferret said. "Many people still experience stigma and misunderstanding around hepatitis B."

A functional cure could mean fewer years of medication, less anxiety and a lower risk of liver disease progressing towards cirrhosis and cancer. But the researchers stress that scientific advances must go hand in hand with wider testing, earlier diagnosis and treatment, and continued vaccination.

While no single therapy is expected to provide the answer, researchers believe that combining new antiviral and immune-based approaches marks the start of a new chapter in hepatitis B research, shifting the focus from controlling the disease to curing it.

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