TuSalud

At Last, Strong Evidence That Treating Hep C Offers Major Benefits

Scientists have firmly established an association between direct-acting antiviral treatment and a lower risk of liver cancer and death.

February 13, 2019 By Benjamin Ryan

Five years have passed since the approval of Gilead Sciences' Sovaldi (sofosbuvir) ushered in the modern era of direct-acting antiviral (DAA) treatment for hepatitis C virus (HCV). During that time, the virus has become readily curable with relatively short courses of a host of different highly tolerable drug regimens. And yet despite all the fanfare over the potential of DAAs to eradicate the virus, which can cause cirrhosis, hepatocellular carcinoma (HCC, the most common form of liver cancer), liver failure and death, scientists have yet to convincingly determine whether these medications are actually linked to a reduced risk of such negative health outcomes.

Until now.

A group of French researchers, following a cohort of more than 10,000 of their countrymen living with HCV, has finally established powerful evidence that treatment with DAAs is associated with a reduced risk of death and liver cancer.

These findings strongly back universal treatment of hepatitis C. They also amount to a forceful response to a controversial 2017 paper published in the Cochrane review in which investigators reviewed data from 157 HCV trials and found no evidence to support or refute DAAs' contribution to the risk of various illnesses and death. That paper was met with an immediate firestorm of criticism from the hep C treatment and research communities.

In October 2018, another team of investigators published a systematic review of 42 studies in an effort to determine how treating hep C affects the risk of liver cancer. The scientists were unable to detect whether HCV treatment was associated with a change in the risk of such a severe health outcome. However, they did find that the post–hep C treatment risk of developing liver cancer was relatively low among those who had never had such a malignancy and very high among those who had already been treated for liver cancer.

Some observational studies have concluded that treating hep C with DAAs or with now-obsolete interferon-based regimens is linked to a lower risk of liver cancer, liver-disease complications and death. But only a handful of studies of people with HCV have compared health outcomes between

those treated and not treated for the virus.

A major new longitudinal study

The new study, published in the prestigious journal The Lancet, is the first prospective longitudinal study to assess health outcomes among people with hep C based on whether they received DAAs. It included a cohort of 10,166 French individuals living with hep C, about three quarters of whom were treated with DAAs during follow-up.

The cohort members were drawn from the ANRS CO22 Hepather cohort, which began recruiting participants in August 2012. People coinfected with HIV were excluded from the cohort. None of those with hep C were coinfected with hepatitis B virus (HBV).

This study excluded those who had a history of decompensated cirrhosis (the more advanced form of the severe liver disease) and liver transplantation. Because people who fall into either of these categories are at the highest risk of suffering complications from hep C, their exclusion might have led the study to underestimate how DAA treatment benefits health outcomes among them in particular.

The study also excluded those who were treated with interferon or ribavirin after their entry into the cohort.

Given the fact that proper follow-up data were missing for 271 cohort members, the analysis focused on 9,895 people who had hep C upon entering the study. This included 3,045 people with cirrhosis (who were followed for a cumulative 1,578 years) and 6,850 people who did not have cirrhosis or who had fibrosis (liver scarring) that was unclassified (this group was followed for 11,131 cumulative years). Note that cirrhosis is synonymous with severe fibrosis.

Details about the cohort members

A total of 7,344 participants received DAAs during the study, including 2,823 people with cirrhosis (followed for 6,320 cumulative years) and 4,521 without cirrhosis or with unclassified fibrosis (followed for 7,306 cumulative years). Meanwhile, 2,551 people were not treated for hep C, including 222 with cirrhosis (followed for 1,578 cumulative years) and 2,328 without cirrhosis or with unclassified fibrosis (followed for 11,131 cumulative years).

Those who received treatment began DAAs a median 4.3 months following their entry into the cohort and were followed for a median 33.4 months after starting the medications. The untreated cohort members were followed for a median 31.2 months.

Compared with those in the untreated group, those in the treated cohort were older, more likely to be men, had a higher body mass index (BMI) and were more likely to report a history of excessive alcohol use. Receiving DAAs was also strongly linked to liver disease severity and other health problems, which is only logical given the increased urgency of treating hep C among those with poorer liver-related health.

In the treated group, 129 people died of any cause during follow-up, including 48 from liver-related causes, 61 from non–liver-related causes and 20 from unclassified causes. A total of 187 people who received DAAs developed liver cancer, and 74 were diagnosed with decompensated cirrhosis.

Among those who were not treated, 89 people died, 25 of them from liver-related causes, 53 from non–liver-related causes and 11 from unclassified causes. There were 71 diagnoses of liver cancer and 32 diagnoses of decompensated cirrhosis among those who did not receive DAAs.

The analysis

The study authors adjusted the data on the cohort members to account for differences between them according to a host of variables that might have influenced health outcomes. This included age, sex, BMI, route of infection, fibrosis severity, whether they'd been treated for HCV before, viral genotype, alcohol consumption, diabetes, high blood pressure, the results of various liver-health tests and the severity of cirrhosis (specifically the MELD score) among those with that condition.

Compared with not receiving the medications, receiving DAAs was associated with a 52 percent reduced risk of death from any cause, including a 41 percent reduced risk of liver-related death. DAAs were also linked to a 40 percent reduction in non–liver-related death, although this finding was not quite statistically significant, meaning it could have been driven by chance. Additionally, hep C treatment was associated with a 34 percent reduction in the risk of liver cancer. DAAs were not linked to any significant change in the likelihood of developing decompensated cirrhosis.

Looking only at the participants who began the study with cirrhosis, the study authors found that receiving DAAs was associated with a 34 percent reduced risk of death from any cause, a 72 percent lower risk of liver-related death, a 60 percent lower risk of non–liver-related death and a 43 percent lower risk of liver cancer. As with the overall cohort, DAAs were not linked to a change in the risk of decompensation for those with cirrhosis.

An analysis that considered only the participants who did not have cirrhosis when entering the cohort did not find any statistically significant association between receiving DAAs and the risk of death, liver cancer or decompensation.

The study authors conducted a further analysis, looking at the entire cohort, of the likelihood of these three health outcomes based on variations in certain study participant characteristics, including:

- Age. Compared with those who were younger than 50 years old, those:
  - 64 years old and older were 2.02 times more likely to die.
  - 56 to 63 years old and at least 64 years old were 2.41 times and 3.47 times more likely to develop liver cancer, respectively.

    - 56 to 63 years old were 2.08 times more likely to develop decompensation.
- BMI. Compared with those withanormalBMI of 18.5 to 24.9, thosewithaBMI of:
    - 5 or lower (indicating they were underweight) were 2.57 times more likely to die.
    - 25 to 29.9 (indicating they were overweight but not obese) were 1.92 times more likely to develop decompensation.
- Genotype. Compared with those with genotype 1 of hep C (the most common genotype in the study and in the United States), those with:
    - genotype 3 (considered the most difficult to treat) were 2.27 times more likely to develop liver cancer and 1.68 times more likely to develop decompensation.
- Fibrosis severity. Compared with those with moderate, mild or no fibrosis, those with:
    - advanced fibrosis were 5.03 times more likely to develop liver cancer.
    - cirrhosis were 3.69 times more likely to die and 9.01 times more likely to develop decompensation.
- Hypertension. Compared with those without high blood pressure:
    - those with high blood pressure were a respective 1.51, 1.44 and 1.6 times more likely to die, develop liver cancer and develop decompensation, respectively.
- Anemia. Compared with those without anemia:
    - those with anemia were 2.45 times more likely to die and 2.1 times more likely to develop decompensation.

Who was cured of hep C?

Of the 7,344 people who started DAAs, 5,615 (76 percent) achieved a sustained virologic response 12 weeks after completing therapy (SVR12, considered a cure). A total of 341 people (5 percent) did not achieve an SVR12, while the cure status of 709 people (10 percent) was unknown. The SVR12 status of an additional 679 cohort members (9 percent) could not be established because of insufficient follow-up time (they were considered still on treatment at the end of the study period).

Consequently, of the 5,956 people whose SVR12 status was known and who had sufficient follow-up time, 5,615 (94 percent) were cured of hep C.

Compared with those in the untreated group, those in the treated but not cured group had a 2.23-fold greater likelihood of being diagnosed with liver cancer during follow-up. There was no evidence of a greater risk of such a cancer diagnosis while cohort members were receiving DAAs, regardless of whether they were later cured.

Conclusions and caveats

“Our results support urgent treatment of patients with advanced liver diseases and extension of the follow-up of treated patients with less severe disease to assess the long-term clinical effect of direct-acting antiviral treatment,” the study authors concluded.

In an essay accompanying the study in The Lancet, Raymond T. Chung, MD, the director of the Liver Center at Massachusetts General Hospital, wrote that the new paper “offers substantive evidence that cure of HCV delivered by all-oral direct-acting antiviral regimens is associated with clinical benefits. These findings firmly counter those of a Cochrane review of direct-acting antiviral treatment trials that could neither confirm nor reject if direct-acting antivirals had an effect on long-term HCV-related morbidity and mortality.”

The new paper’s findings, Chung continued, “also provide the best evidence to date to support guidance documents that recommend direct-acting antiviral treatment for all patients with chronic HCV infection. Finally, they provide credence to the achievability of the goals set out by [the World Health Organization], not only to eliminate HCV but also to substantially reduce its complications.”

The study is limited in part by the fact that follow-up time was relatively limited, meaning the researchers could not determine how DAA treatment affects the risk of the various negative health outcomes over the long term. However, the study authors believe that their finding regarding HCV treatment’s association with major health benefits among those with cirrhosis during such a short period indicates that more follow-up time would not likely change such conclusions.

© 2026 Smart + Strong All Rights Reserved.
http://beta.docker.tusaludmag.com/article/last-strong-evidence-treating-hep-c-offers-major-benefits