

Treatment with DAAs reduces the risk of mortality in the first 18 months after the completion of treatment

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For the first time, a large study has demonstrated that treatment with direct-acting antivirals (DAAs) significantly reduces mortality rates among people with hepatitis C virus (HCV) mono-infection. The study – published in *Clinical Infectious Diseases* – matched people who received therapy with all-DAA regimens with untreated controls. Mortality rates in the first 18 months after therapy were significantly lower among individuals who received DAAs. After controlling for other factors, treatment with DAAs was associated with a 57% reduction in the risk of death.

“To our knowledge, this is the first large-scale study to demonstrate the effect of newer DAA regimens upon survival,” write the authors. “Treatment with 2 commonly used DAA regimens...was associated with significant improvements in survival within the first 18 months of treatment, compared with demographically and clinically similar untreated HCV-infected controls.”

DAAs have revolutionised the treatment of people with HCV, with all-oral regimens achieving sustained virologic response (SVR) – or cure – rates in excess of 90% in clinical trials. Successful treatment with DAAs in routine care has already been shown to be associated with a lower risk of fibrosis progression. However, the survival benefit from successful DAA therapy has never been examined in a large study.

A recent Cochrane Collaboration systematic review concluded that, due to the lack of long-term follow-up studies, there was no evidence that DAAs prolonged life or reduced liver-related ill-health in people who achieved SVR to DAA treatment. The Cochrane review has been strongly criticised by European and United States associations of liver experts for ignoring the short-term nature of the studies of DAAs designed for registration and for ignoring previous evidence from the treatment of hepatitis C, which showed that achieving SVR to interferon-based treatment was associated with a reduction in the risk of death and liver disease.

Investigators from the ERCHIVES (US Electronically Retrieved Cohort of HCV Infected Veterans) study compared survival between people treated with one of two all-DAA regimens – paritaprevir/ritonavir/ombitasvir/dasabuvir (PrOD) and ledipasvir/sofosbuvir (LDV/SOF) – and matched HCV-infected untreated controls.

Individuals with HIV, hepatitis B virus and liver cancer were excluded from the study, as were people without baseline HCV viral load measurements or FIB-4 measurements of liver disease.

The study populations consisted of 6970 people treated for at least 14 days (5497 of whom received LDV/SOF) and an equal number of untreated HCV-infected controls.

Median age was approximately 61 years and approximately 96% of individuals were male. Ninety-four per cent of those treated with LDV/SOF and 90% of those treated with PrOD achieved SVR.

There were some significant differences between the treated individuals and the controls. Those receiving DAAs were more likely to be obese and have liver cirrhosis, but less likely to have serious kidney disease, drug or alcohol dependence and anaemia.

In the first 18 months of follow-up, mortality was significantly higher ($p < 0.001$) among the untreated controls (2.5%) compared to either treatment group (PrOD, 0.3%; LDV/SOF, 1.4%).

Treatment with either regimen was associated with a 57% reduction in mortality (HR = 0.43; 95% CI, 0.33-0.57). Comparison between individuals who received therapy showed that attainment of an SVR was associated with a 43% reduction in the risk of mortality (HR = 0.57; 95% CI, 0.33-0.99).

Between 17 and 20% of treated people had a history of drug or alcohol abuse. This was not associated with lower chances of survival. "Our results suggest that a history of these conditions should not deter providers from initiating treatment," comment the investigators.

"Treatment for HCV with either PrOD or LDV/SOF and attainment of SVR are associated with a significant reduction in mortality, a benefit that is seen within the first 18 months of treatment," the authors conclude. "Benefits of treatment at a population level are expected to be substantial."

References

Butt, AA et al. *Effect of paritaprevir/ritonavir/ombitasvir/dasabuvir and ledipasvir/sofosbuvir regimens on survival compared with untreated hepatitis C virus-infected persons: results from ERCHIVES*. Clin Infect Dis, online edition. DOI.10.1093/cid/cix364.