Interferon-free Therapy for Chronic Hepatitis C

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About 2 per cent of the world's population) has been infected with HCV, of whom an estimated 1.2 per cent (100 million) are living with chronic infection in 2015. In the Global Burden of Disease study published in Lancet last year, HCV infection was recognised as the leading cause of cirrhosis, liver cancer, liver failure, liver transplantation and liver-related deaths worldwide. Many more people suffer morbidity from the extra-hepatic manifestations of HCV infection.

All of these complications are preventable by early diagnosis and treatment, including counselling and management of the lifestyle factors associated with progression to cirrhosis (alcohol, drug use, obesity) and eradication of HCV with antiviral therapy.

There are many contraindications to the currently funded treatment regimens involving the use of interferon, age over 60 years being a significant one as the HCV-infected population ages. As a result, only about 40 per cent of people infected with HCV are considered suitable for current treatments. This number will continue to diminish as the infected population gets older. The combination of pegylated interferon and ribavirin also produces many adverse effects, which limits the completion rate of treatment courses and the efficacy of this treatment in the real world.

As a result, the IFN-containing treatments will never have an impact on the global burden of liver disease caused by hepatitis C in New Zealand. The newer all-oral, direct-acting antiviral agent (DAA) regimens offer considerable hope. If made available and funded in a timely fashion, their greatly superior cure rates and patient suitability offer the prospect of eliminating hepatitis C within our lifetime.

There are now three all-oral regimens able to cure HCV in more than 95 per cent of patients with chronic HCV infection.

The first all-oral regimen to be approved was the 12-week Harvoni regimen (Gilead Sciences). Harvoni is a fixed-dose combination of two DAAs which target different steps in HCV replication – sofosbuvir, a nucleoside polymerase inhibitor, and ledipasvir, a non-structural protein 5A [NS5A] inhibitor). This is effective against HCV Genotype (GT) 1, 2, 4, 5 and 6 with reduced efficacy against GT 3.

The second regimen is 12 or 24-week Viekira Pak (AbbVie). Viekira Pak comprises paratevir, a protease inhibitor boosted by ritonivir, ombatisvir, an NS5A inhibitor and dasabuvir, a non-nucleoside polymerase inhibitor. This si effective against GT 1 and 4.

A third regimen, which is expected to be approved by the FDA and EMA later this year, is the 12 or 16-week M2 regimen (Merck). This is a fixed-dose combination of grazoprevir, an NS3 protease inhibitor and elbasvir, an NS5A inhibitor) and is effective agaist GT 1, 4, 5 and 6.

All of these three regimens are well tolerated, with treatment discontinuation rates of only 1 per cent. These new all-oral DAA regimens are also safe and efficacious in previously difficult-to-treat populations, including patients with HIV co-infection, renal failure or decompensated HCV cirrhosis, and liver transplant recipients with recurrent HCV infection. Under development, are triple DAA regimens including next

generation agents which are expected to provide pangenotypic, shorter duration therapy for all patients with HCV.

Access these all-oral regimens should dramatically increase treatment uptake and will prevent most complications and liver-related deaths in patients with HCV. Widespread access should also reduce new cases of infection, and, if combined with other efforts to prevent disease transmission, like needle exchange, opiod substitution therapy and safe blood donation supply, should eliminate HCV within our lifetime.