Only just the beginning of the end of hepatitis C

2014 marks the 25th anniversary of the identification of the hepatitis C virus (HCV). HCV infection continues to be a major global health problem. Unlike many chronic diseases, hepatitis C can be cured, but it is difficult to treat, not all patients are responsive, side-effects can be severe, and progression to end-stage liver disease and liver cancer is common. Over the past few years, new medicines for HCV infection have begun to transform the treatment landscape, and, just in the past few months alone, the development of new regimens has been so successful that disease experts are heralding an era where all patients can be cured, even debating whether eradication is possible. HCV has six major genotypes and the infecting genotype determines the treatment response and duration. Genotypes 1–3 have a worldwide distribution, but genotype 1 predominates in North America, Europe, and Japan, hence pharmaceutical research to treat this genotype has been prefered to others.

The new treatment modalities are once-daily oral combination regimens with optional inclusion of ribavirin and pegylated interferon (peginterferon) free, so multiple tablets and injections are no longer needed. The novel agents are known as direct-acting antivirals (DAAs). In two phase 2 clinical trials published last week, the DAAs, sofosbuvir and daclatasvir, and the investigational DAAs, ABT-450, ABT-267, and ABT-333 in combination with known protease inhibitors, were shown to achieve high viral clearance response rates (83–100%) in previously treated and previously untreated patients with HCV genotype 1 with a short duration of therapy (12 weeks vs 48 weeks), together with a favourable safety profile compared with the current standard peginterferon based treatments.

Patients with HCV genotypes 2 and 3 also responded well to treatment and there was minimal need for clinical and laboratory monitoring. Testing of other promising DAAs is underway. Results are expected within the next 2 years. Rapid regulatory approval of sofosbuvir in the USA and Europe (and an expedited review of daclatasvir) have been accompanied by reports of promises from companies to ensure that access is achieved as quickly as possible. But given 90% of the estimated 184 million people with hepatitis C live in low-income and middle-income countries, how available and accessible will these new medicines be globally?

The main drawback of these new agents is the huge price tag, which will make treatment out of reach for people in the developed and developing world. Indeed, current treatment uptake is also impeded by cost. One 12 week course of sofosbuvir will cost US$84 000, even though the scientist involved in formulating sofosbuvir, Raymond Schinazi, estimates costs at just US$1400. An even lower price was shown by Andrew Hill and colleagues in a recent study. Based on the fact that the new hepatitis C treatments are comparable in molecular structure and chemistry to HIV antiretrovirals, the authors used the same market dynamics to determine the minimum cost to manufacture them, which was US$100–250 per 12 week treatment course; they concluded that at these low prices, widespread access to these new medicines is feasible within 15 years. Although manufacturers are likely to offer low-income countries steep discounts, around 75% of people with hepatitis C live in middle-income countries regarded as emerging markets by companies, and so are unlikely to benefit from the kind of discounts needed to make treatment available. Interestingly, the sofosbuvir patent application is currently under challenge in India, and if upheld will allow Indian generic drug companies to enter the market and drive major price reductions as seen with HIV/AIDS medicines.

The other concern is the limited testing of these new treatments on less common genotypes and marginalised populations disproportionately affected by HCV infection. For example, there has been minimal testing among those co-infected with HIV. Although the field is likely to see pan-genotypic treatments that clear all genotypes, and will also remove the need for a complex diagnostic, many countries are still years away from these scenarios.

The need for a global plan for hepatitis C is imperative. It should include research and operational priorities, and establish global funding mechanisms. Countries are only likely to develop national plans for hepatitis C when treatments become more affordable. Last year, Tido von Schoen-Angerer and colleagues in a Lancet letter rightly argued that UNITAID—which has successfully lowered prices of HIV treatments—should do the same for hepatitis C medicines. Lessons from HIV/AIDS will be instructive for the hepatitis C field, as will political and community mobilisation to ensure these treatments reach those in most need. ■ The Lancet