Protease Inhibitors in Hepatitis C: From Chronic Disease to Cure

The recent publication of two controlled trials on boceprevir and three on telaprevir heralds a new era for hepatitis C therapy. Boceprevir and telaprevir are the first protease inhibitors for hepatitis C virus to inhibit replication and are referred to as direct acting antiviral agents (DAAs). They are highly potent against most genotypes of hepatitis C virus (HCV) and are highly effective in combination with pegylated interferon and ribavirin. A new major advance in treatment for patients with chronic hepatitis C virus infection. Boceprevir and telaprevir are the first protease inhibitors for hepatitis C virus (HCV) to inhibit replication and are referred to as direct acting antiviral agents (DAAs). They are highly potent against most genotypes of hepatitis C virus (HCV) and are highly effective in combination with pegylated interferon and ribavirin. A new major advance in treatment for patients with chronic hepatitis C virus infection. These new drugs clearly represent a major therapeutic advance in the treatment of chronic hepatitis C. As one would expect the improved effectiveness and safety profile is associated with an economic price tag. The cost of the drug for a single course of therapy has been estimated to be approximately $30-40,000. Although this is a large financial burden, it is worth noting that in the United States the average cost of treating a patient with inflammatory bowel disease is approximately $34,000 per year.

Boceprevir and telaprevir are both protease inhibitors and are used in combination with pegylated interferon and ribavirin. They are most effective against genotype 1 HCV, which is the most common genotype in the United States and Europe. HCV genotype 1 is also the most difficult to treat, with high rates of failure and relapse. In patients with genotype 1, the combination of boceprevir and pegylated interferon/ribavirin (P/I/R) resulted in significantly improved sustained virological response (SVR) rates compared to standard therapy. SVR rates of 50% to 70% were reported in patients treated with boceprevir. These improvements in cure rates for a chronic, and potentially life threatening condition, it would be unfortunate if these drugs were not made available to Irish patients. Consideration of innovative funding models and/or changes in resource allocation may be required. One option would be to consider some form of risk sharing with the pharmaceutical companies concerned. For example the state could consider paying only for patients who achieve a sustained virological response. This would represent the advantage of paying only for patients who were cured. From the pharmaceutical industry point of view revenue could be maximised by optimising the number of patients with sustained viral clearance.

In terms of resource allocation we may have to look at how resources are spent in the management of hepatitis C. To date resources are concentrated on chronic follow up and monitoring for complications. Perhaps it is time to focus on early identification, treatment and prevention of complications. Early identification of those at risk for complications such as cirrhosis, and/or fibrosis, should not to be long term follow up and could be discharged from the liver clinic. Similarly patients who are non-responders to therapy should be monitored closely. Considering patients with hepatitis C attend drug treatment clinics. This group rarely receive anti-viral therapy but represents the bulk of the population at risk for complications. Finally, there are no data on long term outcomes of treatments, linked to methadone treatment, in Ireland. It is very effective in ensuring compliance. The drug treatment infrastructure already exists, widening its remit to include hepatitis C treatment is a logical advancement.

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The new protease inhibitors present the Irish healthcare system with new opportunities and challenges. The challenge is to cure the maximum number of patients at least possible our resources can be directed to reducing the terrible morbidity and mortality of this life-threatening infection to serious disease eradication. In particular we need to effectively target the hard to treat patients, who are at most risk of developing end stage liver disease and the associated complications.

Conflict of interest
The senior authors declare receiving consultancy fees from Merck Sharp & Dohme, Janssen-Cilag Ltd and Bayer Ltd has received funding for clinical research studies from Astellas Ltd, Novartis Ltd and Bayer Ltd.

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