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 therapy1. Boceprevir and telaprevir are the first protease inhibitors (PIs) to be approved for treating hepatitis C virus (HCV) infection. They are both potent and specific inhibitors of the NS3/4A viral protease, and when used in combination with pegylated interferon and ribavirin, they are used in the treatment of chronic hepatitis C. The use of PegIntron and Rebetron have been followed by multiple studies showing high rates of sustained virological response (SVR). To our knowledge, these are the first new major advance in treatment for patients with chronic hepatitis C virus infection in almost two decades. It is significant to be aware of some of the clinical features of hepatitis C virus infection. Firstly, hepatitis C exposure leads to development of antibodies which can be detected in up to 80% of infected individuals. The most vulnerable to hepatitis C are intravenous drug users, and individuals with a history of transfusion of blood and blood products. It is estimated that the rate of chronic infection in approximately 70% of patients. Over time (years or decades) this may lead to chronic hepatitis, cirrhosis, liver cancer and even death. The risk of developing liver cancer increases slowly.

Would be to consider some form of risk sharing with the pharmaceutical companies concerned 2. The price of therapy is not yet fixed but estimates vary from €20,000 to €30,000 for a treatment course. These new drugs clearly represent a major therapeutic advance in the treatment of chronic hepatitis C. As one would expect the improved efficacy comes with an economic price tag. The price of therapy is not yet fixed but estimates vary from €20,000 to €30,000 for a treatment course. These estimates do not include the ancillary costs including pegylated interferon, ribavirin, erythropoietin, viral assays, clinical visits and supportive care services. Without service afford to provide these new treatments? Given the striking improvements in cure rates for a chronic, and potentially life threatening condition, it would be unfortunate if these drugs were not made available to all patients. Consideration of innovative funding models and/or changes in insurance allocation may be required. One alternative we would be to consider some form of risk sharing with the pharmaceutical companies concerned. 3. For example the state could consider paying only for those patients who meet the criteria for a SVR. From the pharmaceutical industry point of view revenue could be maximised by optimising the patient population who are cured. In common with most western countries genotype 1 is dominant in Ireland. The third important feature is that sustained virological response (SVR) appears to equate to viral cure. In patients who have previously not responded to standard therapy, or who are pegylated interferon and ribavirin for 48 weeks with sustained virological response rates of 35%-50%. Because of the rapid development of viral resistance with monotherapy both boceprevir and telaprevir are used in combination with pegylated interferon and ribavirin, although the dosage schedules and duration of treatment vary. In naïve patients sustained virological responses of between 67% and 75% were reported with both drugs compared to 40% and 44% in the standard treatment arms. In patients who had previously not responded to standard therapy, or who had relapsed, SVR of 60% to 65% were reported. This improvement in SVR is very impressive but comes at the expense of an increased side effect profile. Significant anaemia and dysglycemia were common with boceprevir whereas rashes and pruritus were frequent with telaprevir. Both are powerful drugs with complex dosing schedules and stopping rules and should not be prescribed without appropriate expertise and support systems in place. For the patients these are demanding treatment regimens but early stopping rules may mean shorter treatment courses for some individuals.

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 eradication of hepatitis C. In the era of the liver transplant, there are no controls on liver transplantation for patients with hepatitis C and, like other health systems, Ireland is unable to offer a liver transplant to every patient who might benefit. If hepatitis C was a new disease, we would have to consider some form of risk sharing with the pharmaceutical companies concerned. 4. For example the state could consider paying only for those patients who meet the criteria for a SVR. From the pharmaceutical industry point of view revenue could be maximised by optimising the patient population who are cured. In common with most western countries genotype 1 is dominant in Ireland. The third important feature is that sustained virological response (SVR) appears to equate to viral cure.

The new protease inhibitors present the Irish health system with new opportunities but also new challenges. The challenge is to cure the maximum number of patients and to eradicate the virus. It is important 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

No authors have received 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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References

18. It is a clinical and economic question whether the increment is worth the additional cost. An alternative view could be to consider some form of risk sharing with the pharmaceutical companies concerned. 4. For example the state could consider paying only for those patients who meet the criteria for a SVR. From the pharmaceutical industry point of view revenue could be maximised by optimising the patient population who are cured. In common with most western countries genotype 1 is dominant in Ireland. The third important feature is that sustained virological response (SVR) appears to equate to viral cure.
19. On a lighter note a recent study suggests that drinking 3 or more cups of coffee a day significantly increases SVR rates with standard anti-viral therapy. If confirmed this may offer an additional, low cost, method of boosting viral clearance rates.
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