

EDITORIAL

## Disruptive therapeutic innovation and the opportunity to eliminate a chronic disease – The issue of chronic hepatitis C in Spain

The availability of direct antiviral agents (DAAs) in Spain for the treatment of hepatitis C virus (HCV) infection since April 2015 fits into the theory of disruptive innovation. According to this concept, first formulated by Professor Clayton Christensen in 1995 (1), radical or disruptive innovation eventually makes profound changes in society by introducing simplicity, convenience, accessibility, and affordability in sectors where previously existing conditions are associated with barriers, high costs, and/or some sort of restrictions. Recent examples of disruptive innovation include GPS navigation assistance devices and tactile smartphones.

Greater accessibility to DAAs allowed coverage for candidates traditionally labeled as “difficult to treat” with interferon-based therapies (e.g., advanced or decompensated liver disease, elderly patients, autoimmune disease, major depression, chronic renal failure, patients on dialysis, transplant receivers, HCV-HIV coinfection). These individuals represented an “untreated” group that can now afford treatment, which is a key criterion in the definition of disruptive development. Currently, the “difficult-to-treat” concept no longer exists, as all subgroups consistently achieve sustained virological response rates (SVRs) higher than 90% with shorter, easier treatments with excellent tolerability. As a result, the number of treated patients has risen from 9,800/year to almost 90,000/year since the publication of the Spanish Ministry of Health (MSSSI) Strategic Plan in May 2015 (2), and since DAAs were made available.

The clinical benefit for all HCV patients, including those previously considered inappropriate candidates, is indisputable (3-6). However, the Spanish Royal Decree 16/2012 establishes that funding decisions in our country must be guided by scientific evidence, cost-effectiveness, and economic assessment criteria. As any increase in health effectiveness provided by therapeutic innovations may also substantially raise the cost, the cost-effectiveness analysis estimating this increase in cost per unit of health gained, as compared to previous technologies, should also be part of the economic assessment. However, this information alone is insufficient to decide on NHS reimbursement (7), since how much the NHS is willing to invest per unit of effectiveness gained is also a factor. The measure of effectiveness most frequently used in health economic evaluations is the Quality-Adjusted Life Year (QALY). The cost-effectiveness per QALY threshold in our country has been recently estimated in €21,000-€24,000 (8), hence any amount lower than this threshold would make an intervention “profitable”. In this issue of the *Spanish Journal of Gastroenterology (Revista Española de Enfermedades Digestivas)*, Turnes et al. (9) report the data from a Markov analysis, including a decision tree and lifetime modeling, in a cohort of 51,900 HCV Spanish patients with significant fibrosis (stage F2-F4) who were treated with DAAs between 2015 and 2016. The authors compare two scenarios, pre-DAA vs post-DAA, and apply a sensitivity analysis to test the robustness of the model.

The results show that DAAs had a significant clinical impact, decreasing liver-associated mortality by 58%, cirrhosis decompensation by 63%, hepatocellular carcinoma (HCC) development by 53%, and hepatic transplantation by 59%. Overall, these figures represent a saving of €468 million. It is noteworthy that real-practice results in our country reflect those obtained in pivotal clinical trials (2-6). This similarity between efficacy and effectiveness is rarely observed with drug innovations. Although the overall cost of the post-DAA strategy was €376 million higher as compared to the pre-DAA approach, the excellent clinical results and cost savings obtained with the DAA-based strategy make this investment worthwhile. In addition, this is reflected in savings of 153,971 QALYs, which means that the incremental cost-effectiveness ratio (ICER) obtained is €2,441/QALY. This figure is well below the efficiency threshold calculated for Spain (€21,000-24,000/QALY) (6). Conversely, this “good investment” is also reflected in the analysis of the monetary value of the QALYs earned, and in a conservative scenario, an efficiency threshold of €20,000 would result in a saving of €3,079 million in terms of QALYs gained.

The authors estimate an annual discount of 3% in their model, and their analysis shows an incremental cost of €218 million. However, the cost of hepatitis C treatment in Spain has gradually decreased over time, as this investment was €1,066 million, €600 million, and €200 million in 2015, 2016, and 2017, respectively (10). In addition, the lower cost of the new-generation DAAs recently approved in Spain would further reduce the incremental cost and increase the efficiency of the continuation and/or extension of treatment strategies presented at the SPCHC. Furthermore, a shorter duration of treatment might decrease monitoring load and number of physician visits, as well as leave days and absenteeism.

In summary, the results from this cost-utility analysis represent an additional, important piece of information to strengthen universal HCV treatment policy. The funding of this plan has proven an excellent investment in public health, and an important step forward to render chronic hepatitis C a residual disease over the next few years in Spain.

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