Ledipasvir/sofosbuvir for the treatment of chronic hepatitis C: a cost-effectiveness analysis across different genotype-1 clinical subgroups

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BACKGROUND AND OBJECTIVES

Chronic Hepatitis C (CHC) affects approximately 160 million people worldwide [1] and represents the major cause of chronic liver disease, end-stage cirrhosis and liver cancer [2]. Pegylated interferon plus ribavirin (P+R) has been the standard of care for CHC, but it is contra-indicated in several groups of patients [1] and only a variable proportion of P+R eligible patients achieve sustained virological response (SVR) [3]. Boceprevir (BOC) or telaprevir (TVR) plus P+R in HCV genotype-1 patients has failed to achieve generalized market acceptance, in part due to the approval of newer, more efficacious and safer options. Sofosbuvir (SOF), a pan-genotypic inhibitor of the hepatitis C virus (HCV), has been approved for use in CHC patients, with unprecedented sustained virologic response rates and tolerability profile [4]. More recently, the combination of SOF and ledipasvir (LDV) – a new HCV inhibitor with potent antiviral activity, namely in genotype-1 – has resulted in higher rates of SVR [5]. The objective of this analysis was to assess the cost-effectiveness of LDV/SOF fixed-dose combination for the treatment of HCV genotype-1 in Portugal.

METHODS

Costs and effectiveness were based on a CHC natural history evolution Markov-type model accounting for the presence of cirrhosis and previous treatment experience for HCV genotype-1 infected individuals (Figure 1). The model incorporated 13 health-states: 5 Metavir fibrosis score states (F0 = no fibrosis, F1 = portal fibrosis without septa, F2 = portal fibrosis with rare septa, F3 = numerous septa without cirrhosis, and F4 = compensated cirrhosis), 2 SVR states (with and without cirrhosis) and 3 advanced liver disease states (decompensated cirrhosis, hepatocellular carcinoma and liver transplant) – Figure 1. A figure with an average age of 39.5 years and a Metavir distribution of F2: 10%, F3: 40% and F4: 50% was considered.

For experienced treated patients, the model allowed the comparison of LDV/SOF against absence of treatment and combination therapy with P+R and BOC+P+R, irrespective of clinical subgroup (circrhotic or non-cirrhotic). For treatment naive patients, the model allowed the comparison of LDV/SOF against absence of treatment and combination therapy with P+R, BOC+P+R, SOF+P+R and SOF+R, irrespective of clinical subgroup (Table I).

The analysis considered the Portuguese National Health System (NHS) perspective. The choice of comparators was based on identical therapeutic indication and financing status by the Portuguese NHS (except for SOF which was considered the standard of care). Drug costs were taken from official NHS price lists, with the exception of the costs for SOF and LDV/SOF (provided by Gilead Sciences). Hepatitis C health-state related resource utilization and cost estimates were reviewed by an expert panel. No indirect costs were considered. Values for health-related quality of life (HRQoL) utilities were identified from literature [6] and adjusted for pharmacologic treatment [7] (Table II).

Annual discount rates were set at 5% for both costs and effectiveness following the guidelines of the Portuguese Health Authority. Results are expressed in incremental costs per life year (LY) and quality-adjusted life year (QALY) gained.

RESULTS

Overall LDV/SOF is expected to result in benefit increments between 0.21 and 6.80 LY (0.26 and 5.80 QALY) depending on the clinical subgroup and comparator, with costs ranging from savings of 56,881 € to increments of 23,288 € per patient. Incremental cost-effectiveness ratios (ICER) vary between LDV/SOF dominance and a maximum of 10,563 €/LY (9,098 €/QALY) – Table III.

In the comparison against SOF+P+R or SOF+R, LDV/SOF was shown to be dominant, while versus boceprevir regimens ICERS varied between 1,896 €/LY (2,597 €/QALY) (experienced cirrhotic) and 10,563 €/LY (9,098 €/QALY) (experienced non-cirrhotic). When LDV/SOF was compared against PegIFN+RBV, the ICER variation was 3,828 €/LY (5,396 €/QALY) (naïve cirrhotic) to 8,042 €/LY (6,776 €/QALY) (experienced non-cirrhotic). All ICERS were found to be below commonly accepted cost-effectiveness thresholds.

CONCLUSION

Ledipasvir/sofosbuvir is expected to represent good value for money including cost-saving scenarios in the treatment of CHC genotype 1 in Portugal, irrespective of the clinical subgroup comparator.

Table I: Modelled regimes and respective sustained virological response estimates.

Table II: HR-QoL utility values for the different health-states in the model.

Table III: Cost-effectiveness results of LDV/SOF for HCV genotype-1 infected patients.

Figure 1: Markov state-transition diagram for chronic hepatitis C and liver disease.

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