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Brief report

Cost-effectiveness analysis of sofosbuvir-simeprevir regimens for chronic hepatitis C genotype 1 patients with advanced fibrosis☆

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ABSTRACT

Background and objective: The aim of this study was to measure the cost-effectiveness of the treatment with simeprevir and sofosbuvir in chronic hepatitis C genotype 1 patients with F3-F4 levels of fibrosis, according to the results of the COSMOS trial.
Material and methods: A Markov model was used to estimate the costs and clinical outcomes from the start of therapy. In the model, the progression was simulated alongside the different health states of the chronic liver disease associated with chronic hepatitis C using whole life as time-horizon.
Results: The 12-weeks treatment schemes was below the threshold of €40,000 per quality-adjusted life year. On the contrary, despite the 50% cost reduction, the 24-weeks regimen demonstrated a limited level of efficiency when compared with the willingness to pay used in the Spanish medical literature.
Conclusions: This finding would support the introduction of a flat rate in the price of drugs without taking into account the duration of treatment to ensure that treatment with 24 weeks was efficient.

Análisis coste-efectividad del tratamiento de la hepatitis C crónica con sofosbuvir-simeprevir en pacientes con genotipo 1 y fibrosis avanzada

Palabras clave:
Hepatitis C
Sofosbuvir
Simeprevir
Coste-efectividad

RESUMEN

Introducción y objetivo: El objetivo de este estudio fue medir la relación coste-efectividad del tratamiento con simeprevir y sofosbuvir en pacientes con hepatitis C crónica genotipo 1 y grados de fibrosis F3-F4, de acuerdo con los resultados del ensayo clínico COSMOS.
Material y métodos: Se utilizó un modelo de Markov para estimar los costes y los resultados clínicos desde el comienzo del tratamiento. Usando como horizonte temporal toda la vida del paciente, en el modelo se simuló la progresión de la enfermedad entre los diferentes estados de salud de la enfermedad hepática crónica asociada a la hepatitis C.
Resultados: Los regímenes de 12 semanas se situaron por debajo del umbral de 40.000 €/año de vida ajustado por calidad. Por el contrario, aun con una reducción del 50% del coste de adquisición, el régimen de 24 semanas demostró un nivel de eficiencia en el límite del requerido por la disponibilidad a pagar utilizada en la literatura médica española.
Conclusiones: Este último dato justificaría la introducción de un coste igual para la duración de 12 y 24 semanas, asegurando la eficiencia del tratamiento de duración prolongada.

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Introduction

Treatment of hepatitis C virus (HCV) infection is experiencing continuing progress in recent years, obtaining sustained viral responses over 90%.[1] However, its high price limits its widespread use. Therefore, the economic evaluation of all clinical scenarios is becoming a determining factor in the incorporation process into clinical practice.

In HCV infected patients with high degree of fibrosis, the use of free-interferon schemes with direct acting antivirals (DAAs), such as Simeprevir (SIM) and sofosbuvir (SOF), is recommended. Given the limited resources, treatment has been prioritized for patients with higher risk of morbidity and mortality (patients with advanced fibrosis or compensated cirrhosis, transplant recipients and those with severe extrahepatic manifestations of HCV infection), since they obtain greater benefit in the short term.[2]

The SIM-SOF combination is indicated in patients with HCV genotype 1 with high levels of fibrosis (F3-F4), providing high efficiency and preventing from adverse effects associated with interferon treatment. The regimen used has varied depending on the duration (12 or 24 weeks) and the addition or not of ribavirin.[3]

The aim of the study was to measure the cost-effectiveness of SOF-SIM treatment in patients with HCV genotype 1 and levels of F3-F4 fibrosis according to COSMOS clinical trial results.[3]

Methodology

A cost-effectiveness analysis was conducted to calculate the incremental cost-effectiveness ratio, which is a measure of contrast between increased costs and increased effectiveness among the different therapeutic alternatives compared.[4]

The basis of the study was COSMOS clinical trial, in which the effectiveness of the SIM-SOF combination was analyzed.[3] It included patients with genotype 1 and with advanced fibrosis (F3-F4).[3] Patients in each cohort were randomized to receive SIM-SOF with or without ribavirin for 12 or 24 weeks.

Markov model[5] was used, previously described and validated[6,7] to estimate the costs and clinical outcomes from the start of treatment. In this model, the natural history of hepatitis C was simulated, including death from liver disease or any other causes (Fig. 1), using the TreeAge Pro 2014 software. The patient's life was used as time horizon to estimate quality-adjusted life years (QALY) and costs. The treatment cohort population was defined in accordance with the average characteristics of patients in the clinical trials, 50 years old, and assuming a distribution of 50% of patients in F3 and another 50% in F4. The discount rate applied was 3%.[8] The perspective applied was that of the Spanish National Health System assuming an effectiveness threshold in €40,000 per QALY.[4,8] This model is fully described in the technical annex attached, available online.

Given the absence of comparator arm in the COSMOS study, the standard of care was used as an alternative for genotype 1 with F3-F4 fibrosis consisting of triple therapy with peginterferon, ribavirin and a generic protease inhibitor resulting from combining boceprevir with telaprevir.[7,9] This treatment provided a 72% sustained viral response with an overall laboratory sale price of €33,000.

Drug costs were estimated depending on the dosage and treatment regimen included in the clinical trial and the data sheet from the laboratory sale price (Table 1). Since the acquisition of both drugs in our environment is subject to considerable discount compared to the official price due to the competition among the therapeutic alternatives, a sensitivity analysis reduced the price by 50%. Cost estimates considered a SOF regimen 400 mg/day, SIM 150 mg/day, and ribavirin dosage depending on body weight.

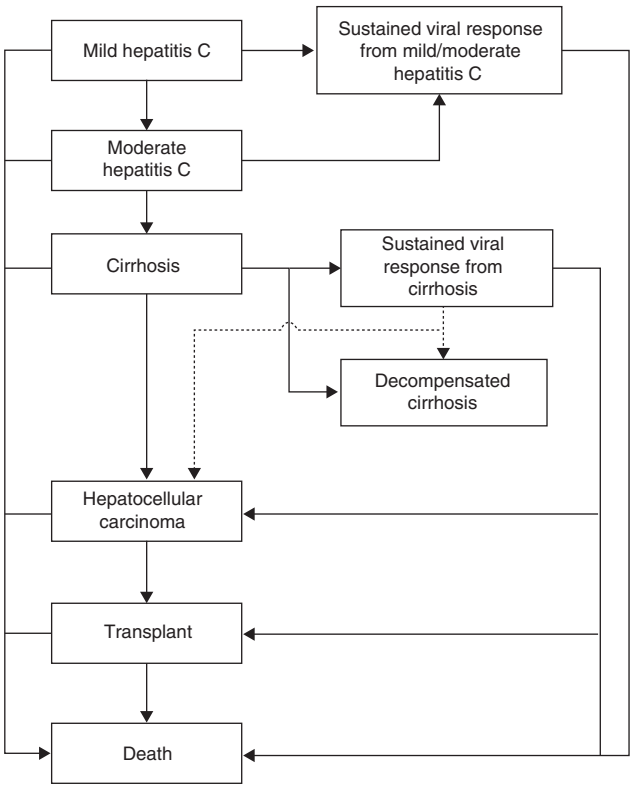

Fig. 1. Conceptual model of the natural history of liver disease associated with hepatitis C virus.

Health resources costs associated to disease progression were obtained from hospitals in the Basque Health Service in 2013.

The model included health-related adjustment for quality of life[6,7] for the various stages of chronic liver disease (Fig. 1). This model also considered the loss of quality of life associated with treatment (disutility) as a result of the adverse effects.[6,7] To analyze the uncertainty of results the following was conducted: (a) sensitivity analysis by varying the discount (0–5%), (b) effectiveness of the SOF-SIM (−5%) combination and (c) the baseline cohort (100% F3 and 100% F4) and probabilistic sensitivity analysis (ASP), which is the method recommended by the NICE. All of this was conducted with pharmacy costs reduced by 50%.[4–7] The PSA analyzes simultaneously the impact on the results of parametric uncertainty associated with the evidence available on effectiveness, utilities, hospital costs and the transition probabilities among different stages.

Results

Table 1 shows the results for the four branches of the COSMOS clinical trial. The 12-week regimens are below €40.000 per QALY threshold with the official price, and even cheaper with the price calculated using a 50% discount over the price of drugs. Probabilistic analysis showed consistent results, and in the 12-week regimens the percentage of efficient simulations or below the €40.000 per QALY threshold ranged from 95 to 99%. As in other studies, the variable with the greatest impact in the univariate analysis was the discount.

Discussion

The main contribution of our paper is to establish the cost-effectiveness ratio of the 12-week SIM-SOF combination, which is