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ORIGINAL ARTICLE

# Cost–effectiveness analysis of sofosbuvir, peginterferon and ribavirin in patients with chronic hepatitis C: Early treatment in the initial stage of fibrosis vs. delayed treatment in advanced fibrosis☆

**María Buti**[a,b], **Raquel Domínguez-Hernández**[c,*], **Itziar Oyagüez**[c], **Miguel Ángel Casado**[c]

[a] *Unidad de Hepatología, Hospital Universitario Vall d'Hebron, Barcelona, Spain*
[b] *Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Spain*
[c] *Pharmacoeconomics & Outcomes Research Iberia, Madrid, Spain*

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**KEYWORDS**
Chronic hepatitis C;
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**Abstract**
*Aims:* Cost–effectiveness analysis of sofosbuvir combined with peginterferon alpha-2a and ribavirin (SOF/Peg-IFN/RBV) in early versus advanced fibrosis in previously untreated patients with chronic hepatitis C genotype 1 (CHC-GT1), from the perspective of the Spanish National Health System (NHS).
*Methods:* A Markov model was developed to compare lifetime costs and outcomes (life years gained [LYGs] and quality-adjusted life years [QALYs]) of 2 treatment strategies: SOF/Peg-IFN/RBV administered during early fibrosis (mild-moderate fibrosis; F2–F3) or advanced fibrosis (cirrhosis; F4). Efficacy (sustained virologic response), annual transition probabilities, disease management costs and utilities were obtained from the literature. Costs and outcomes were discounted annually at 3%. Direct costs were considered, expressed in Euros (€, 2014). Probabilistic sensitivity analysis (PSA) was also performed.
*Results:* SOF/Peg-IFN/RBV therapy at F2–F3 was more effective (19.12 LYGs and 14.14 QALYs) compared to F4. In a cohort of 1000 patients, SOF/Peg-IFN/RBV prevented 66 cases of decompensated cirrhosis, 60 hepatocellular carcinomas and 4 liver transplantations compared with therapy in advanced fibrosis. The total lifetime cost of early therapy (€ 43,263) was less than the cost of treatment in the advanced stage (€ 49,018). Early therapy was a dominant strategy, more effective and less costly in all simulations. In the PSA analysis, administration of SOF/PEG-IFN/RBV at F2–F3 was dominant in all simulations.

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* Corresponding author.
*E-mail address:* rdominguez@porib.com (R. Domínguez-Hernández).

*Conclusions:* Starting SOF/Peg-IFN/RBV therapy at F2–F3, compared with therapy at F4, reduced the incidence of liver disease complications and was associated with cost savings for the Spanish NHS in CHC-GT1 patients.


**PALABRAS CLAVE**
Hepatitis C crónica;
Genotipo 1;
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Coste-efectividad

**Análisis coste-efectividad de sofosbuvir, interferón pegilado y ribavirina en pacientes con hepatitis crónica por virus C: tratamiento precoz en fases iniciales de fibrosis vs. tratamiento tardío en fases avanzadas**

**Resumen**
*Objetivo:* Análisis coste-efectividad de sofosbuvir con peginterferón/ribavirina (SOF/PEG-IFN/RBV) en pacientes con hepatitis C crónica genotipo 1 (HCC-GT1) no tratados previamente con diferentes grados de fibrosis, desde la perspectiva del Sistema Nacional de Salud (SNS).
*Métodos:* Modelo de Markov para estimar costes y resultados en salud (años de vida ganados [AVG] y años de vida ajustados por calidad [AVAC]), con una tasa de descuento del 3% anual de dos estrategias: SOF/PEG-IFN/RBV en fases precoces (fibrosis leve-moderada, F2-F3) o tardías (cirrosis compensada, F4). La eficacia (respuesta virológica sostenida), probabilidades anuales de transición, costes del manejo de la enfermedad y utilidades se obtuvieron de la literatura. Se consideraron costes directos expresados en € 2014. Se realizó un análisis de sensibilidad probabilístico (ASP).
*Resultados:* SOF/PEG-IFN/RBV en F2-F3 fue más efectiva (19,12 AVG y 14,14 AVAC) que en F4 (16,36 AVG y 9,27 AVAC). En 1.000 pacientes, SOF/PEG-IFN/RBV en F2-F3 podría evitar 66 casos de cirrosis descompensada, 60 de carcinoma hepatocelular y 4 trasplantes, en comparación con F4. El coste total de la terapia con SOF/PEG-IFN/RBV en F2-F3 (43.263 €) fue menor que en F4 (49.018 €). Administrar el tratamiento en F2-F3 frente a F4 representó una estrategia dominante (más efectiva y con menor coste). En el ASP, la administración de SOF/PEG-IFN/RBV en F2-F3 permaneció dominante en el 100% de las simulaciones.
*Conclusiones:* La administración de SOF/PEG-IFN/RBV en F2-F3, comparada con la terapia en F4, disminuyó la incidencia de complicaciones de la enfermedad hepática y se asoció con un ahorro en costes para el SNS en pacientes HCC-GT1.


## Introduction

Hepatitis C virus (HCV) infection affects around 160 million people worldwide,[1] 9 million of whom live in European countries.[2] Chronic hepatitis C (CHC) is a disease that is asymptomatic in the early stages, but which can evolve to liver cirrhosis as it progresses. Up to 25% of patients with CHC develop cirrhosis,[3] 4% of whom progress annually to decompensated cirrhosis, with an associated risk of approximately 1.6% per year of developing hepatocellular carcinoma (HCC).[3] HCV infection is the main indication for liver transplant, and is estimated to be responsible for 350,000 deaths annually.[4]

Genotype 1 (GT1) is the most common HCV genotype globally,[5] and is responsible for 65.4–76% of cases in Spain.[6,7] Current treatments recommended for patients with HCV GT1 infection are based on oral, direct-acting antiviral therapies free from interferon (IFN).[8]

However, these antivirals are not available in all countries, and even in countries where they are marketed, situations arise that make it difficult for patients to access treatment.[9] In some settings, treatment is only reimbursed in patients with cirrhosis, so patients with mild fibrosis are treated with IFN-based regimens, or must wait until the disease progresses[10] in order to meet healthcare system criteria for receiving subsidised IFN-free therapy.[11]

The criterion of sustained virologic response (SVR)—defined as absence of HCV RNA levels detectable in serum at the end of 12 weeks of treatment[12]—is widely accepted and recognised as indicative of therapeutic success.[12,13]

The clinical benefits associated with the SVR criterion are evident at several levels. Patients who achieve SVR have a life expectancy similar to that of the general population,[14] since it is related with a substantial reduction in overall mortality.[15,16] Furthermore, an SVR is associated with regression of liver fibrosis, even in patients with mild cirrhosis,[17] with a subsequent reduction in the risk of developing HCC.[18] However, this risk is not completely eliminated in patients with cirrhosis, even if they have responded satisfactorily to treatment.[19–21]

The efficacy of antiviral therapy in patients with advanced fibrosis or cirrhosis is significantly lower than in patients with mild fibrosis, resulting in a lower likelihood of achieving an SVR.[22,23]