Ledipasvir/Sofosbuvir (LDV/SOF) treatment of naïve patients with mild chronic hepatitis C (CHC) genotype 1 (GT1) compared to patients with significant fibrosis: is it a cost-effective therapy?

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Background

- Direct Acting Antivirals in patients with chronic hepatitis C (CHC) have shown high efficacy in genotype 1 (GT1).
- Spanish National HCV Plan prioritizes therapy of patients with significant fibrosis (≥F2). However, early diagnosis and treatment are important to prevent disease complications and to eliminate HCV infection[1].
- Ledipasvir/Sofosbuvir (LDV/SOF) for 8-24 weeks is a recommended treatment for HCV GT1 patients. Therapy duration depends on the presence of cirrhosis, baseline viral load and treatment experience. LDV/SOF for 8 weeks is the recommended for GT 1 naïve patients without cirrhosis[2].
- Simplified treatment is associated with less monitoring and has been seen to be associated with improved adherence[3].

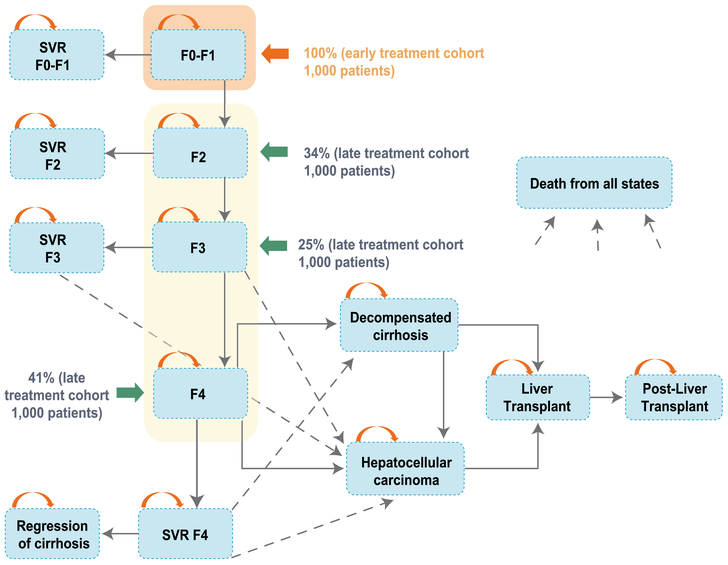
Objective

The aim of the study was to estimate the cost-effectiveness and cost-utility of LDV/SOF treatment in GT1 naïve patients with mild or no fibrosis (F0-F1) compared with those with significant fibrosis or cirrhosis (≥F2) from the Spanish National Health System perspective.

Methods

- A Markov model was developed to simulate the natural course of CHC infection comparing both treatment initiation options for two cohorts of 1,000 patients with an average age of 52 years[4] (Figure 1).
- In the early treatment cohort, 100% of patients started into F0-F1 states. Patients with significant fibrosis are distributed across the fibrosis states, according to proportions observed in Spanish population with CHC (34% F2, 25% F3 and 41% F4)[4].
- The effectiveness of therapy was measured as sustained virologic response (SRV) rate based on real-world evidence[5-6] after 12-weeks of the end of treatment (Table 1).
- The duration of treatment of F0 to F3 patients was determined according to HCV viral load.
  - Patients with a viral load <6 million UI/mL (94,25%)[7] received 8 weeks of therapy .
  - Patients with ≥6 million UI/mL (5,75%)[7] received 12 weeks of therapy.
- It was assumed that all patients completed only one course of treatment and retreatment was not evaluated.
- The annual transition probabilities were obtained from published studies[8-13], and adjusted annually based on the mortality by age range[14].

Figure 1. Markov diagram for chronic Hepatitis C



F0-F1: METAVIR liver fibrosis score, absence or mild fibrosis; F2: METAVIR liver fibrosis score, moderate fibrosis; F3: METAVIR liver fibrosis score, severe fibrosis; F4: METAVIR liver fibrosis score, compensated cirrhosis. SVR: Sustained Virological Response.

Methods

- Patients with disease stages F0-F1 and F2 who achieved an SVR were considered "cured" of viral and hepatic disease.
- Patients with disease stages F3 and F4 who attained a SVR could progress to hepatocellular carcinoma (HCC). Probability of cirrhosis regression was considered for patients with F4 and SVR.
- Utility values obtained from the literature were applied to the different health states[15].
- The analysis considered only direct health costs (€, 2015): drug costs were based on the published local list prices[16] with applicable mandatory deductions (7.5%)[17] (€3,622.92/weekly), monitoring costs and disease management for each health state[10,18] (Table 1).
- The model estimated costs, Life Years Gained (LYG) and Quality-Adjusted Life Years (QALY) over patients' lifetime. A 3% discount rate was applied to costs and outcomes[19].
- A Probabilistic Sensitivity Analysis (PSA) was performed to assess the robustness of the model.

Table 1. SVR12 rates, unit cost (€, 2015) and utilities for the base case

SVR12 rates for each fibrosis states (%)		
Health states	**Treatment duration**	
	8 weeks[3]	**12 weeks[3-4]**
F0-F1	96.94%*	97.52%*
F2	95.00%	95.57%
F3	96.88%	95.36%
F4	—	88.00%
Health states	**Annual costs[17-18]**	**Utility values[13]**
F0-F1	€265.12	0.98[†]
F2	€282.58	0.92
F3	€282.58	0.79
F4	€558.06	0.76
SVR from F0-F1	€112.75	1.00
SVR from F2	€112.75	0.92
SVR from F3	€112.75	0.86
SVR from F4	€449.32	0.83
Regr. C	€112.75	0.86[‡]
DC	€2,272.52	0.69
HCC	€6,656.00	0.67
LT	€122,075.31	0.5
Post-LT	€17,841.48	0.77

DC: Decompensated Cirrhosis; HCC: Hepatocellular carcinoma; LT: Liver transplant; Regr. C: Regression of cirrhosis; SVR: Sustained Virological Response. *A weighted for SVR from F0-F1 rate (8-12 weeks). †The average utilities estimate from F0 and F1 states. ‡The same annual utility scores that SVR F3

Results

- LDV/SOF in patients with F0-F1 was a dominant strategy (less costly and more effective).
- Treatment initiation with LDV/SOF in patients at stages F0-F1, is more effective (19.85 LYG and 19.80 QALY) than initiation at stage ≥F2 (18.63 LYG and 16.25 QALY), generating cost-savings of €9,228.49 per patient (€3,661 due to disease management and monitoring) (Table 2).
- In a cohort of 1,000 HCV patients, LDV/SOF treatment in patients with F0-F1 avoided 40 cases of decompensated cirrhosis, 59 hepatocellular carcinoma, 6 liver transplant and 78 liver-related deaths compared with the same therapy for patients with ≥F2 (Figure 2).
- The PSA, conducted using a Monte Carlo simulation with 5,000 runs, showed that LDV/SOF therapy at early fibrosis stages (F0-F1) was a dominant strategy in 100% of the simulations (Figure 3).

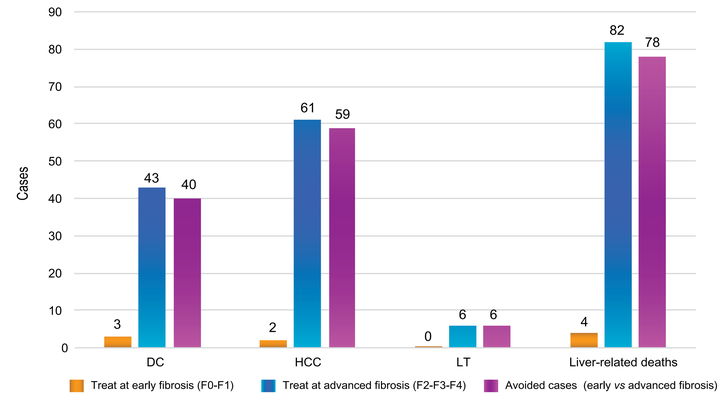
Table 2. Base case results analysis (per patient)

	Treatment of mild fibrosis (F0-F1)	Treatment of significant fibrosis (F2-F3-F4)	Incremental difference (mild vs significant fibrosis)
Life Years Gained	19.85	18.63	1.22
QALY	19.80	16.25	3.54
Average total cost	€30,822.51	€40,050.99	€-9,228.49

LYG: Life-years gained; QALY: Quality-adjusted life-years

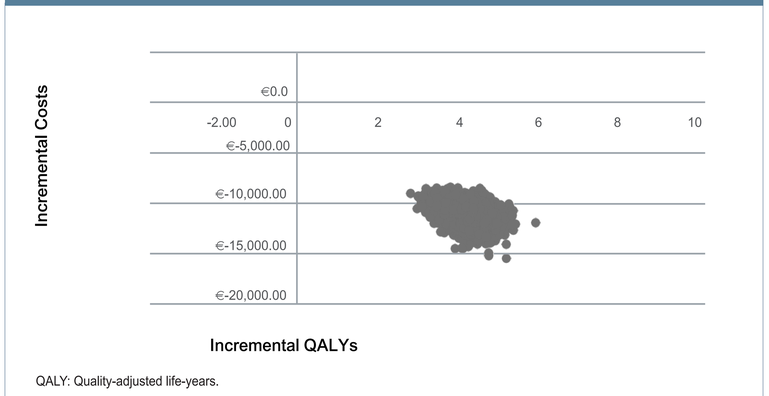
Results

Figure 2. Predicted liver-related complications in relation to therapy of patients with mild fibrosis vs. significant fibrosis



DC: Decompensated Cirrhosis; HCC: Hepatocellular carcinoma; LT: Liver transplant.

Figure 3. Cost-effectiveness plane (treatment in early fibrosis *vs.* significant fibrosis)



QALY: Quality-adjusted life-years.

Conclusion

- Therapy with LDV/SOF in CHC GT1 naïve patients with mild or no fibrosis (F0-F1) is cost-effective, providing more benefit in terms of LYG and QALY, reducing the incidence of liver complications and generating cost-savings to the NHS, compared to the treatment in patients with significant fibrosis (≥F2).
- This study shows the benefit of treating patients in early fibrosis stages, supporting the access to treatment of less advanced patients.

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