Early versus delayed use of sofosbuvir plus peginterferon/ribavirin therapy in fibrosis patients with hepatitis C virus: a cost-effectiveness analysis

M. Buti[1], R. Domínguez-Hernández[2], I. Oyagüez[2], M. Rueda[3], MA. Casado[2]

[1]Hospital Vall' d'Hebrón, Barcelona, Spain; [2]Pharmacoeconomics & Outcomes Research Iberia, Madrid, Spain; [3]Gilead Sciences, Madrid, Spain.

Background

- The administration of treatment in patients with chronic hepatitis C virus (HCV) infection in different disease stages is associated with a variation in the therapy's effectiveness.
- The early diagnosis and HCV-therapy are important for reducing the incidence of liver complications of progressive disease for patients with chronic hepatitis C (CHC)[1].

Objetive

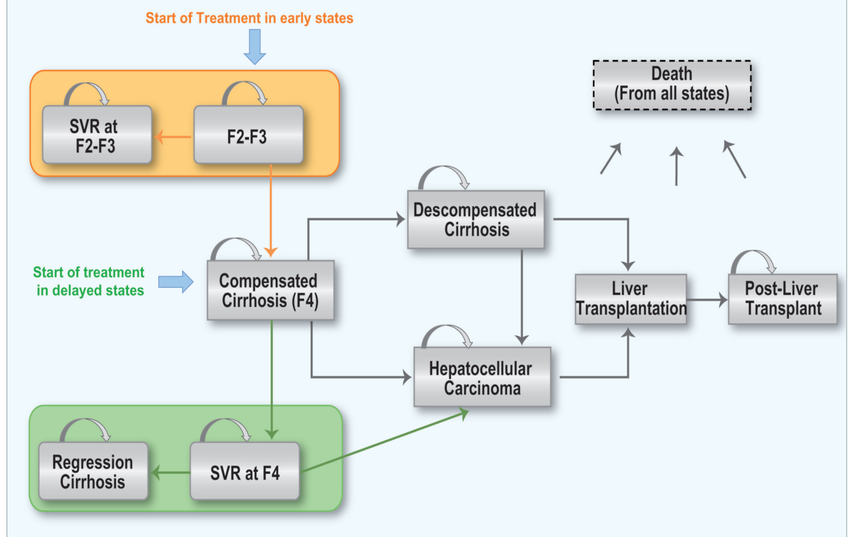
The aim of the analysis was to assess the cost-effectiveness of sofosbuvir combined with peginterferon alfa-2a plus ribavirin (SOF/PEG-IFN/RBV) at early versus delayed fibrosis disease stage, in previously untreated patients infected with HCV genotype 1.

Methods

- A Markov model with ten health states was developed to compare lifetime cost and outcomes (life years gained-LYG and quality-adjusted life years-QALY) of two treatment strategies: early SOF/PEG-IFN/RBV at mild-moderate fibrosis (F2-F3) or delayed treatment at compensated cirrhosis (F4).
- The efficacy data was measured as sustained virologic response (SVR) at 12-weeks after therapy completion (based on NEUTRINO study)[2]: 91% (F2-F3) y 81% (F4)[3].
- In absence of disaggregated data, no discontinuation therapy due to lack of efficacy or adverse events was assumed.
- Patients in "SVR at F4" state were allowed to transit to regression of cirrhosis or hepatocellular carcinoma (HCC).
- Patients who achieved "SVR at F2-F3" or "cirrhosis regression" were considered cured and therefore they had the same life expectancy as the general population.
- Annual transition probabilities were obtained from published sources[4-8] and adjusted with specific mortality by age[9] (mean age: 52 years).
- From the Spanish National Health System perspective, only direct cost (pharmaceutical, and disease cost by health state) were included. Cost were expressed in Euro (€) 2014.
- Drug cost for the SOF/PEG-IFN/RBV 12-weeks regimen was calculated based on available local ex-factory prices[10] with applicable mandatory deductions for marketed drugs[11].
- Disease management costs[12,13] and utilities values[14] by health state were based on literature (Table 1).
- A 3% annual discount rate was applied to costs and health benefits[15].
- Deterministic and probabilistic sensitivity analysis (PSA) were performed to assess the model robustness.

Methods (Cont.)

Figure 1. Markov Model



SVR: Sustained Virologic Response. F2-F3: mild-moderate liver fibrosis (Metavir stage)

Table 1. Unit costs (€, 2014) and utilities

Drug costs (ex-factory price[10] with mandatory deduction[11])	Weekly cost
SOF (Sovaldi®, 400 mg/day)	€ 3,237.50
PegIFN-2a (Pegasys®, 180 µg/week)	€ 177.07
Generic RBV (1,000 mg/day (<75kg), 1,200mg/day (≥75kg))*[16]	€ 130.22

Health states	Utilities[14]	Annual cost[12-13]
F2-F3	0.71	€ 241.92
SVR at F2-F3	0.77[ᵀ]	€ 0.00
F4	0.55	€ 449.32
SVR at F4	0.59[ǂ]	€ 449.32
Regression of cirrhosis	0.59[‡]	€ 0.00
Decompensated cirrhosis (DC)	0.45	€ 1,532.73
Hepatocelluar carcinoma (HCC)	0.45	€ 7,019.17
Liver Transplant (LT)	0.45	€ 143,647.97
Post liver transplant (post-LT)	0.67	€ 14,863.97

*43.8% patients <75kg and 56.2% ≥75kg. [ᵀ] Average utility of F2 and F3 states. [ǂ] The same increase in quality of live that from F2-F3 to SVR at F2-F3. [‡]The same utility that SVR at F4.

Results

- Early SOF/PEG-IFN/RBV therapy at F2-F3 was more effective (14.14 QALY) than delayed treatment at F4 (9.27 QALY) (Table 2).
- In a 1,000 patients cohort, SOF/PEG-IFN/RBV at F2-F3 could avoid new cases of liver disease complications compared to delayed therapy in F4 patients (Table 2).
- Total cost of early therapy at F2-F3 with SOF/PEG-IFN/RBV was lower than the cost of delayed treatment in F4 (Table 2).

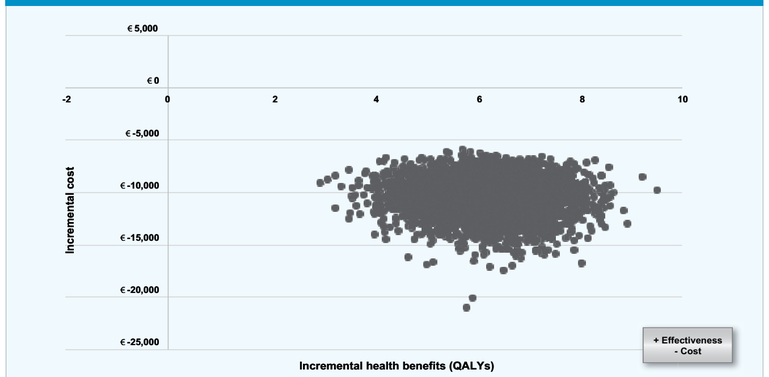
Table 2. Base case results analysis

	F2-F3	F4	Difference (Incremental)
Life years gained (LYG)	19.12	16.36	2.76
Quality Adjusted Life Years (QALY)	14.14	9.27	4.87
Total cost	€ 43,263.44	€ 49,018.85	€ -5,755.41
Health States	**Number of cases**		**Avoided cases (F2-F3 vs F4)**
Cases of DC	38	104	-66
Cases of HCC	17	77	-60
Liver Transplants	1	5	-4

DC:Descompensated Cirrhosis. HCC: Hepatocellular Carcinoma.

- Early versus delayed SOF/PEG-IFN/RBV therapy was a dominant strategy (more effective and less costly).
- In PSA, with 5,000 Montecarlo simulations, early use of SOF/PEG-IFN/RBV remained dominant in 100% of simulations (Figure 2).

Figure 2. Cost-effectiveness plane



Conclusion

Initiating SOF/PEG-IFN/RBV treatment at early fibrosis stages (F2-F3) compared to delayed administration of therapy at F4, in previously untreated patients infected with HCV genotype 1:

- Reduce the incidence of new cases of liver-disease complications and it is associated to cost savings for the Spanish National Health System.
- It is a cost-effective strategy (more effective and less costly) in the treatment of patients with CHC.

Disclosure

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Author MB declares have not any conflict of interest.

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