THE AVAILABILITY OF DIRECT ACTING ANTIVIRALS (DAA) IN 2012: A FRENCH MODEL-BASED ANALYSIS OF THE INCREASED NUMBER OF PATIENTS TREATED FOR CHRONIC HCV INFECTION

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Abstract

Background: In 2012, genotype 1 (G1) HCV-infected patients will be treated with the association of pegylated interferon (PEG-IFN), ribavirin (RBV) and a DAA namely a protease inhibitor (PI) with a substantially higher efficacy. Evaluating the impact of this new association availability on HCV-treatment prescriptions is crucial for resource allocation, planning and treatment optimization.
Aim: To estimate the number of G1 patients to be treated with the new association of PEG-IFN/RBV/PI in France in 2012.
Methods: We used a published model of HCV progression to predict the number of patients to treat in 2012 according to their fibrosis score and treatment history status. Data on PEG-IFN sales (2002-2009) were used to calibrate the model; we assumed that the proportion of G1 patients treated with PEG-IFN in 2010/2011 was similar to 2009. We estimated the number of patients to treat in 2012 under 3 scenarios based on HCV screening rate and the proportion of screened patients treated: 1) HCV screening rate unchanged vs. 2010; proportion of treated F0-F1 patients unchanged, proportion of treated F2-F4 patients increased to the current proportion of treated F2-F4 genotype 2/3 (G2/3) patients; 2) Scenario 1 but the proportion of treated F0-F1 patients increased to the current proportion of treated F0-F1 G2/3 patients; 3) Scenario 2 but 5%-increase in HCV screening rate.
Results: Assuming a HCV screening rate of 62% at the end of 2011, the number of G1 patients who knew their HCV status was estimated at 47,400 (56% treatment-naive). Table presented the estimated number of G1 patients treated in 2010 and to be treated in 2012.

	Treated with PEG-IFN/RBV in 2010	To treat with PEG-IFN/RBV/PI in 2012		
		Scenario 1	Scenario 2	Scenario 3
Total	5,100	15,000	18,300	19,400
Naïve	3,200	5,500	8,200	9,200
Experienced	1,900	9,500	10,100	10,200

Conclusions: Our model-based estimates indicate that new and more efficacious anti-HCV treatments may result in 9,900-14,300 additional patients to treat in France in 2012, representing a 2- to 3-fold increase in the number of G1 patients who will be treated.

Background

In patients with chronic HCV genotype 1 (G1) infection viral clearance upon current standard of care, pegylated interferon (PEG-IFN) plus ribavirin (RBV) : < 50%.

Promising results recently reported with the addition of protease inhibitors (PIs) to PEG-IFN plus RBV (1).

One can speculate that the availability of these combinations will encourage a large number of treatment-naive and treatment-experienced patients to be treated

- Because of a consequent increase in patients' and their physician's expectation of cure rates with these combinations

The aim of this study: to estimate the number of G1 patients to be treated in France in 2012 with the new association of protease inhibitor added to PEG-IFN plus RBV.

Methods

We simulated the progression of newly infected HCV cohorts during the 1900 to 2011 period from onset of HCV infection to death using an updated published Markov model of HCV natural history (Figure 1) and treatment (2).

We determined the number of HCV-mono-infected patients treated with PEG-IFN plus RBV overtime until January 2012 by calibrating the model with data on the observed overall number of PEG-IFN used in France between 2002 and 2009 (derived from PEG-IFN sales (GERS, 2002-2009) and PEG-IFN used in hepatitis C clinical trials (2005-2009)).

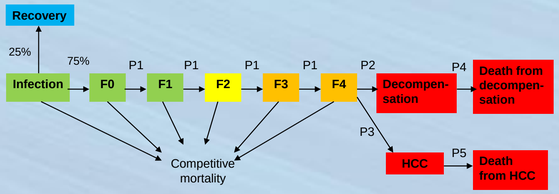
-From this we estimated the annual proportion of treated patients over 2002-2009 period among screened patients aged 18 to 70 years.

We fitted the model to the reported 400,000 HCV prevalence in 2004 (3) and to age-specific annual HCC deaths (http://www.who.int/whosis/mort/download/en/index.html) related to HCV (4).

We projected the number of HCV-infected patients alive at January 2012 based on their knowledge of HCV status, their genotype (G1/4, or G2/3), their fibrosis stage, and their treatment history (treatment naïve vs. treatment experienced).

We finally determined the number of G1-infected patients to be treated with PEG-IFN, RBV plus a PI in 2012 under different scenarios regarding this new combination use in HCV-infected patients:
-Scenario 1 = HCV screening rate unchanged vs. 2010; proportion of treated F0-F1 patients unchanged, proportion of treated F2-F4 patients increased to the current proportion of treated F2-F4 G2/3 patients;
-Scenario 2 = Scenario 1 but the proportion of treated F0-F1 patients increased to the current proportion of treated F0-F1 G2/3 patients;
-Scenario 3 = Scenario 2 but 5%-increase in HCV screening rate during 2011.

Figure 1 – HCV natural history



P1 = Probability of fibrosis progression, dependent of age, sex and alcohol abuse (5)
P2 = Probability of decompensation, dependent of alcohol abuse (6,7)
P3 = Probability of HCC, dependent of age and sex (8)
P4 = Probability of death from decompensation, dependent of time (9)
P5 = Probability of death from HCC, dependent of age and time (10)

Results

1. Estimated proportion of treated patients in France in 2009 among HCV-screened patients aged 18 to 70 years, according to Metavir liver fibrosis scores, treatment history and genotype (Table 1).
2. Projected number of Genotype 1 patients aged 18 to 70 years in 2012 in France stratified by the knowledge of their HCV-infection (screened or not screened), Metavir liver fibrosis scores (F0 to F4), and treatment history (naïves or experienced), assuming either unchanged HCV screening rate when compared to 2010, or a 5%-increase in HCV screening rates during 201 (Table 2).
3. Estimated number of Genotype1 patients treated in 2010 and to be treated in 2012 under the 3 scenarios (Table 3).

Table 1	F0-F1	F2-F4
Treatment-naives		
Genotype 1 or 4	7.5%	13.4%
Genotype 2 or 3	24.0%	42.8%
Treatment-experienced		
Genotype 1 or 4	25.4%	45.3%
Genotype 2 or 3	32.5%	58.1%

Table 2	HCV screening rate unchanged (=62% in 2011)	5%-increase in HCV screening rates (=65% in 2011)
Screened		
Naïves F0-F1	16,600	18,300
Naïves F2-F4	9,900	11,300
Experienced F0-F1	8,200	8,300
Experienced F2-F4	12,700	12,800
Unscreened		
F0-F1	25,500	23,600
F2-F4	20,800	19,200

Table 3	Treated with PEG-IFN plus RBV in 2010	To be treated with PEG-IFN, RBV plus a PI in 2012		
		Scenario 1	Scenario 2	Scenario 3
Total	5,100	15,000	18,300	19,400
Naïve	3,200	5,500	8,200	9,200
Experienced	1,900	9,500	10,100	10,200

Conclusion

With the availability of a new standard-of-care treatment, a substantial additional number of HCV-infected patients will be treated in 2012.

The monitoring and safety management of these new treatments will be different and more complex than PEG-INF plus RBV combinations.

These data should be used by policy makers to prepare 2012 and the arrival of new drugs in terms of budget allocation and organizational issues.

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