COST-SAVING APPROACH TO TRIPLE THERAPY FOR HEPATITIS C USING THE OPTIM PROGNOSTIC TOOL TO PREDICT VIROLOGIC RESPONSE TO 4 WEEKS OF PEGINTERFERON AND RIBAVIRIN IN GENOTYPE 1 PATIENTS

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1. BACKGROUND

In hepatitis C patients receiving boceprevir or telaprevir based-triple therapy, virological response at week 4 of double peginterferon + ribavirin (P+R) therapy could predict the possibility of achieving sustained viral response (SVR).

A prognostic tool has been recently developed to predict rapid viral response (RVR) and/or a decline of 1 $\log_{10}$ HCV-RNA (D1L) at week 4 of double therapy in naïve patients (Box)[1].

Predictive tool for RVR or D1L[1]

$$R_{RVR} = \frac{1}{1+e^{-(0.495 + 1.513 \times \text{Baseline VL} - 0.797 \times \text{Coinfection} + 2.061 \times \text{IL28B} - 0.873 \times \text{HCV Genotype} - 0.345 \times \text{Forns})}}$$

$$R_{D1L} = \frac{1}{1+e^{-(2.909 + 0.630 \times \text{Baseline VL} - 0.719 \times \text{Coinfection} + 2.169 \times \text{IL28B} + 0.657 \times \text{HCV Genotype} - 0.322 \times \text{Forns})}}$$

Variable "Viral Load" (VL) is categorized as follows:
VL < 800 kIU/ml, VL = 1
VL ≥ 800 kIU/ml, VL = 0

Variable "HIV coinfection" is dichotomous:
Coinfection = 1
No coinfection = 2

Variable "IL28B" is dichotomous:
CC = 1
TT; CT = 0

Variable "HCV genotype" is dichotomous:
G1 = 1
G4 = 0

For variable «Forns index» the following calculation is used:
7.811 – 3.131 × ln (platelet count, 10^3/L) + 0.781 × ln (GGT; IU/L) + 3.467 × ln (age; years) – 0.014 × (total cholesterol; mg/dl)

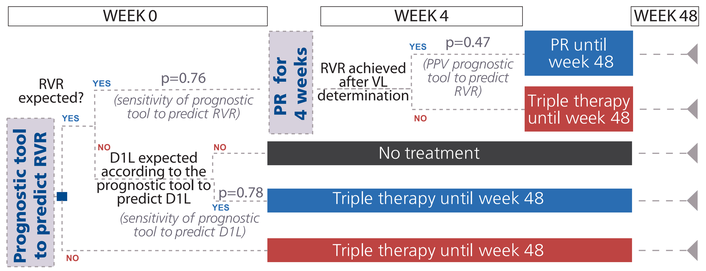
2. AIM

The aim of this study was to assess the economic impact on total costs for different strategies using or not the current tool.

3. METHODS

* A decision tree (Figure 1) was designed based on sensitivity of the prognostic tool to predict RVR and D1L. Time horizon lasted less than 1 year, and therefore no discount rate was applied. Pharmaceutical costs were calculated according to the recommendations in the Summary of Product Characteristics[2], and assuming the whole recommended duration. The study was carried out from the perspective of the Spanish National Health Service.

FIGURE 1. Decision tree



D1L, viral load decrease ≥ 1 log10; PPV, positive predictive value; PR, standard double therapy with peginterferon and ribavirin; RVR, rapid viral response

* Treatment stopping rules were not considered for any of the treatments. Ex-factory prices from GCOF[3] with the 7.5% mandatory rebate[4] were applied to boceprevir, telaprevir and peginterferon, and ex-factory generic price for ribavirin was used.

* Triple therapy costs were calculated as average cost of boceprevir and telaprevir treatments for 48 weeks (€36,218.62).

* A viral load determination at week 4 was applied only to those patients with expected RVR according to the implementation of the prognostic tool to predict RVR. The unitary cost per each determination (€120.54 [year 2013 value]) was obtained from a local health cost database [5].

* Alternative scenarios were tested modifying sensitivity and positive predictive value of prognostic tools with 95% CI limits, and triple therapy costs.

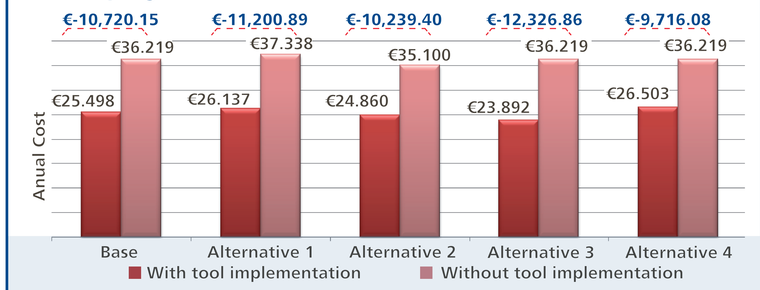
4. RESULTS

* Total cost (2013€) for hepatitis C therapy per patient was estimated to be €36,218.62 in 48 weeks.

* The implementation of the prognostic tool was associated to €10,720.15 savings per patient in the base case scenario.

* The total savings per patient in alternative scenarios ranged from €9,716.08 to €12,326.86 (Figure 2).

FIGURE 2. Cost-analysis results. Total treatment cost for hepatitis C therapy (48 weeks) per patient with or without implementation of the prognostic tool



Alternative scenario 1: Triple therapy cost= €37,337.50; **Alternative scenario 2:** Triple therapy cost= €35,099.74; **Alternative scenario 3:** prognostic tools sensitivity (upper limit 95% CI) and RVR positive predictive value; **Alternative scenario 4:** RVR prognostic tools sensitivity (lower limit 95% CI) and RVR positive predictive value.

Assuming €1,000,000 of fixed budget, the implementation of the prognostic tool would enable a cost reduction of 29.6%, which translates into the treatment of 12 additional patients in the base case scenario within the existing budget.

5. CONCLUSIONS

* **The OPTIM tool could identify patients having a high probability of response to P+R (those with a high probability of achieving RVR) in whom dual or triple therapies are equally effective, and the protease inhibitor may be best reserved for second-line therapeutic use.**

* **In addition, it enables the identification of a subgroup of patients having a low probability of achieving a reduction of HCV-RNA <1 log after 4 weeks of combination therapy (lead-in), in whom the probability of SVR to the current triple therapy is suboptimal.**

* **The implementation of this tool in clinical practice could be a cost-saving strategy compared to the universal triple therapy for hepatitis C, that could contribute to a more efficient allocation of the available resources.**

6. REFERENCES

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