Evaluation of a Predictive Model of Individual Chance for Sustained Virological Response in Patients with Chronic Hepatitis C Treated with Peginterferon alfa-2a and Ribavirin

Mauss S1, Hueppe D2, Zehnter E1, Richter S3, Tappe A3, Herrmann E4

1Center of Gastroenterology and Hepatology, Dusseldorf; 2Center of Gastroenterology, Herne; 3Center of Gastroenterology, Dortmund; 4Klinikum der Johann Wolfgang Goethe Universität, Frankfurt; 5Roche Pharma AG, Grenzach-Wyhlen, Germany

INTRODUCTION

Sustained virological response (SVR) is an endpoint of interest in patients treated with interferon-based antiviral therapy. Treatment decision is often based on the patients baseline characteristics and the evaluation of treatment response in the early phase of therapy.

OBJECTIVE

The objective of this analysis is to evaluate the predictive value of the response calculator for the treatment of CHC-patients in an unselected cohort under routine clinical practice.

METHODS

The data base of this evaluation is part of a large ongoing real life conditions. We applied the proposed response calculator on data of 949 patients treated in various German multi-center clinical trials. These models were proposed using defined baseline factors and, if available, serum HCV RNA at week 4 and week 12 to predict sustained virological response (SVR) for individual patients.

RESULTS

Aim of this analysis was to evaluate the proposed response calculator for the success of the treatment of CHC-patients in an unselected cohort under routine clinical practice.

CONCLUSIONS

Evaluation of a response calculator derived from study data in an unselected cohort showed a lower predictive value than for study patients.

Evaluation of the response calculator in a selected group of patients from the cohort simulating “study conditions” showed better predictive values coming nearer to the original study data.

In routine clinical practice the lack of structured patient selection may result in the introduction of additional factors influencing treatment success and may alter the relative weight of the variables of the response calculator developed in study patients.

Further analysis is necessary to include these factors in the model.

References


Figure 1. Study patients

Table 1: Baseline data

<table>
<thead>
<tr>
<th>Patients treated with Peg + RBV</th>
<th>n=7266</th>
<th>949 patients treated in various German multi-center clinical trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male / female)</td>
<td>61.4%</td>
<td>57.4%</td>
</tr>
<tr>
<td>Age (mean ± SD in years)</td>
<td>42.0 ± 12.0</td>
<td>47.4 ± 12.0</td>
</tr>
<tr>
<td>Duration of infection (mean ± SD in years)</td>
<td>12.1 ± 8.9</td>
<td>16.1 ± 8.9</td>
</tr>
</tbody>
</table>

Evaluation ALL

The SVR rate for all patients (N=7266) was 48.2% (see Figure 2).

The prediction of SVR by the response calculator yielded a specificity of 49% and a sensitivity of 77% (see Figure 3). The predictive behaviour is shown in Figure 4.

Boxplots of predicting SVR vs. Non-SVR are shown in Figure 5.

Evaluation of the model in this cohort yielded an area under ROC of 0.67 (see Figure 6).

Evaluation in defined subgroups demonstrated that these factors were addressed adequately by the algorithm:

- GT 1/2/3/6 vs. GT 4/5: AUC 80% (see Figure 7).
- HCV RNA >400,000 IU/mL vs. ≤400,000 IU/mL: AUC 80%.
- age ≤40 years vs. >40 years: total-cholesterol ≤180 mg/dL vs. >180 mg/dL: AUC 80%
- fibrosis yes vs. no: AUC 80%
- ALT normal vs. high: AUC 80%
- GGT normal vs. high: AUC 80%
- Furthermore, potential factors not included in the prediction showed similar area under ROC values with consistently lower rates of SVR for all analyzed populations.

Further analysis is necessary to include these factors in the model.

Figure 2. Sustained virological response (SVR)

Figure 3. Specificity and sensitivity

Figure 4. Comparing SVR rates with prediction values (ALL)

Figure 5. Boxplots of linear predictor (ALL)

Figure 6. Area under ROC (ALL)

Figure 7. Area under ROC (STUDY)