Patients followed in an addiction medicine clinic are less likely to be eligible to hepatitis C drug studies regardless of drug use

Gabrielle Doré, Julie Bruneau,1,2,3, Valérie Martel-Laferrière1,2,3

1. Université de Montréal; 2. Centre de recherche du Centre hospitalier de l’Université de Montréal; 3. Centre hospitalier de l’Université de Montréal

Background: Phase III trials evaluating direct-acting antivirals (DAA) consistently report high sustained virologic responses (SVR5). The strict eligibility criteria applied to these studies may affect the generalizability to clinical practice. It has been demonstrated that drug use generally does not affect SVR. This retrospective cohort study sought to estimate the proportion of patients followed in a tertiary addiction clinic who would meet eligibility criteria for clinical trials. If drug use was not considered as a exclusion criteria.

Methods: The sample population consists of patients with active HCV genotypes (GT 1-3), seen at the clinic between 01/2013 and 08/2015. Information from clinical charts was retrieved to examine how participants would meet the eligibility criteria of 21 studies. Individual patient’s data were compared with the studies’ eligibility criteria.

Results: A total of 214 patients met the inclusion criteria (GT 1: 58.5%; GT 2: 31.3%; GT 3: 10.2%; GT naïve: 2.0%). A total of 108 patients (M/F) could have been included in at least one study. The most inclusive study was C-EDGE TN: 80/117 (68%). The most frequent exclusion criteria were the presence of significant diseases (cardiac, pulmonary, hepatic or psychiatric conditions and contraindicated medications).

Conclusion: Even without considering drug use, only half of the patients of the addiction clinic would have been eligible for at least one study. This under-representation stems from strict eligibility criteria that promote a healthier population. Our study suggests that the DAA might prove less effective when administered to infected populations followed in specialized clinics for drug use.

Introduction:

• Because phase III studies’ goal is to evaluate efficacy, they are generally recruiting “ideal” patients that don’t necessarily represent the real target population

• Data obtained from these studies are used for treatment recommendations and development of public health strategies/treatment reimbursement policies. These decisions assume that the target population will respond as well as phase III studies’ patients to treatment.

• Drug use is the principal risk factor for HCV acquisition. In Canada, people who use intravenous drugs (PWID) represent 66% of patients infected with HCV, but only 1% of the overall population.

• PWIDs are often sicker than the general population. This may affect their response to treatment.

• Most HCV direct acting antiviral agents (DAA) phase III studies excluded PWIDs.

• The goal of this project was to evaluate the proportion of PWIDs who could have theoretically been included in phase III studies if drug use had not been an exclusion criterion.

Methods:

• Retrospective study conducted with institutional review board approval.

• Inclusion criteria:
  • Adult patients seen at the addiction clinic of the Centre hospitalier de l’Université de Montréal, an urban tertiary care center, between January 2013 and September 2015
  • Infected by HCV genotype 1, 2 or 3, either naïve or experienced to pegylated interferon and ribavirin.

• Exclusion criteria:
  • Genotype 4, 5 or 6 or unknown
  • Reinfection
  • Previous treatment with direct acting antiviral agents


• Eligibility criteria were extracted from each study protocol. If unavailable, companies were contacted to obtain the information, and if still not available, criteria were extracted from clinicaltrials.gov.

• Information relative to trials inclusion/exclusion criteria was extracted from patients’ charts and used to determine patient’s eligibility to trials.

• Genotypes, cirrhosis status and past treatment history were used to determine trials for which a patient could have been part of the target population.

• Because it was part of the study design, drug use was not considered as an exclusion criterion to decide if patients would have been eligible to phase III trials.

• Descriptive statistics were used.

Studies’ general criteria and number of potentially eligible patients before evaluation

<table>
<thead>
<tr>
<th>Genotypes</th>
<th>Naïve</th>
<th>Experienced</th>
<th>No cirrhosis</th>
<th>Cirrhosis</th>
<th>Potential patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>POSTRION</td>
<td>2, 3</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>93</td>
</tr>
<tr>
<td>FUSION</td>
<td>2, 3</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>12</td>
</tr>
<tr>
<td>POLARIS-2</td>
<td>1</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>117</td>
</tr>
<tr>
<td>POLARIS-3</td>
<td>1</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>102</td>
</tr>
<tr>
<td>PEARL-2</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>1</td>
</tr>
<tr>
<td>PEARL-1</td>
<td>1</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>12</td>
</tr>
<tr>
<td>PEARL-IV</td>
<td>1</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>88</td>
</tr>
<tr>
<td>SAPHIRE-I</td>
<td>1</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>102</td>
</tr>
<tr>
<td>TURQUOISE-I</td>
<td>1</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>12</td>
</tr>
<tr>
<td>ASTRAL-3</td>
<td>1</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>117</td>
</tr>
<tr>
<td>POLARIS-2</td>
<td>1, 2</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>131</td>
</tr>
<tr>
<td>POLARIS-3</td>
<td>3</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>22</td>
</tr>
<tr>
<td>C-EDON TN</td>
<td>1</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>117</td>
</tr>
<tr>
<td>C-EDON CD-STAR*</td>
<td>1, 4</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>49</td>
</tr>
</tbody>
</table>

Overall, 108 patients (48%) would have been eligible to at least one study.

Conclusion:

• Even if drug use or opioids substitution therapy had not been exclusion criteria, less than 50% of the patients seen in our addiction medicine clinic would have been eligible to a phase III DAA clinical trials.

• Psychiatric conditions and other medical comorbidities were common exclusion criteria that would have precluded their inclusion in those trials.

• Studies including PWIDs will need to be conducted to evaluate drug effectiveness in this population and companies should aim to include this population in trials evaluating new agents.

Funding:

• Study: No funding
• Valérie Martel-Laferrière is funded by the Fonds de Recherche du Québec en Santé (programme chercheur-boursier clinicien, junior 1)