Viral Escape with Protease Inhibitor "first wave" in Naïve patient, We Should worry about? 

Case Report

Ana Paula Serra Leopércio
MD Infectious Diseases Department
Ambulatório de Hepatites Virais
CRT Santa Cruz – São Paulo
FMABC – URDIP – Santo André

4th Latin American Meeting on Treatment of Hepatitis and HIV Co-infection
20-21 March 2015
Case Report

• 53 year, male, born and live in Carapicuíba – SP, married, construction worker

• Without comorbidities - 89kg, 1,69 cm; BMI: 30,8

• In 2012 - diagnosed: chronic hepatitis C Genotype 1a
  - Pretreatment: Hb: 16,0 ; Plaq: 68.000; alb: 4,2; INR: 1,08 (89%), HCV RNA level: 55.992UI/ml (5.75 logs)
  - Esophageal varices of medium caliber (Endoscopy)
  - Hepatosplenomegaly (Ultrason) - liver biopsy is not necessary
Case Report

⇒ PegIFN alfa, Ribavirin 250mg (5 pills/d) and Telaprevir 375mg (6 pills/d): without Lead in

- Good adherence and tolerability

=> Patient behaved as slow respondor: HCV RNA level at:

<table>
<thead>
<tr>
<th>Week 4</th>
<th>Week 8</th>
<th>Week 12</th>
<th>Week 24</th>
<th>Week 25</th>
</tr>
</thead>
<tbody>
<tr>
<td>40UI/ml*</td>
<td>27UI/ml*</td>
<td>&lt; 12UI/ml*</td>
<td>173UI/ml*</td>
<td>1052UI/ml*</td>
</tr>
<tr>
<td>(1.61 logs)</td>
<td>(1.43 logs)</td>
<td>(&lt;1.08 logs)</td>
<td>(2.24 logs)</td>
<td>(3.02 logs)</td>
</tr>
</tbody>
</table>

Pretreatment: HCV RNA level: 55.992UI/ml (5.75 logs)
* Real-time PCR - abbot HCV Real Time - lower limit 12UI/ml

breakthrough
Case report

- The therapy was suspend => “futility rule”

- The patient recovered uneventfully, except for the frustration in not responding to treatment
Viral Escape with Protease Inhibitor "first wave" in Naïve patient

- Naïve patients chronic HCV genotype 1a → Cirrhotic

Cirrhotic → Treatment Protease Inhibitor "first wave"

Currently scheme in Brasil: Triple Therapy (first wave) Gen1: 70-80% SVR in naïve and relapsers

We should worry about it?

-Virology Failure
Therapy and Existence of mutations chronic hepatitis C

• It has been reported virologic failure with this scheme, even naïve¹

Study in Japan (2013): existence of mutations in patients with untreated

The pre-existing natural resistance in untreated patients with PI¹

Viral escape in *Naïve* patient: We should worry about it?

- Emergence of resistance with the new agents: has been demonstrated in the literature in *naïve* and experienced with DAAs.

- Mutations confer cross-resistance and may lead to virologic failure with triple therapy.

- The prevalence of DAAs-resistance mutations in HCV-infected patients who were not treated with DAAs is *unknown* in many regions.


DAAs-resistance mutations in HCV-infected

• The presence of mutations can guide the best initial regimen of therapy?

  - Future treatments: “2nd and 3rd wave” agents (NS5A, NS5B and polymerase inhibitors), some already approved in the U.S., Europe and Japan

  - So, We should worry about it? What is the real impact of these mutations?
Obrigada!