Supplementary data
Figure S1 is available as Supplementary data at JAC Online (http://jac.oxfordjournals.org).

References
1 EFSA Panel on Biological Hazards (BIOHAZ). Scientific opinion on the public health risks of bacterial strains producing extended-spectrum \( \beta \)-lactamases and/or AmpC \( \beta \)-lactamases in food and food-producing animals. EFSA Journal 2011; 9: 2322.

J Antimicrob Chemother 2012
doi:10.1093/jac/dkr448
Advance Access publication 20 November 2011

Detection of vancomycin levels in patients receiving telavancin but not vancomycin

Michael S. Gelfand, Kerry O. Cleveland* and Kashif A. Memon

Division of Infectious Diseases, Department of Medicine, University of Tennessee Health Science Center, Memphis, TN, USA

*Corresponding author. Tel: +1-901-448-5770; Fax: +1-901-448-5940; E-mail: kcleland@uthsc.edu

Keywords: daptomycin, linezolid, pharmacokinetics

Sir,
Telavancin is a lipoglycopeptide antibiotic with a chemical structure closely related to the glycopeptide antibiotic vancomycin. Telavancin has excellent in vitro activity against methicillin-resistant Staphylococcus aureus and, in the trials which led to its approval for the treatment of skin and soft tissue infections, it was shown to be non-inferior to vancomycin. Renal toxicity is the principal significant adverse effect of telavancin. A standard dose of 10 mg/kg daily is recommended in patients with normal renal function and monitoring of serum or plasma levels is neither recommended nor available commercially. It is not known if telavancin serum levels correlate with the efficacy or renal toxicity of this antibiotic. Perhaps due to a lack of therapeutic superiority data and concerns about renal toxicity, telavancin has yet to be widely used in clinical practice.

Recently, a patient receiving the standard dose of telavancin for a staphylococcal infection was demonstrated to have an apparent detectable serum vancomycin level (after the level was inadvertently ordered by a house officer). This serendipitous finding led us to check vancomycin levels in several other patients with normal renal function who were receiving standard doses of telavancin. No patients had received vancomycin. Trough levels were obtained immediately prior to a dose of telavancin and peak levels were obtained 1 h after the infusion was completed. The vancomycin serum levels were determined by a particle-enhanced turbidimetric inhibition immunoassay method (Synchron LX System, Beckman Coulter, Inc., Brea, CA, USA). The results are shown in Table 1.

We speculate that if a consistent correlation can be established between serum vancomycin and telavancin levels in patients treated with telavancin, a commercially available vancomycin serum level assay can then be used to monitor telavancin therapy, in place of an unavailable telavancin assay, in order to establish possible correlation between telavancin levels and its clinical efficacy and/or renal toxicity. Although telavancin plasma assays were apparently done as part of approval studies, we had no access to a telavancin assay to attempt to establish the correlation. If the manufacturer of telavancin or an independent investigator is able to perform telavancin assays, they may choose to perform such a study.

Funding
This study was carried out as part of our routine work.

Transparency declarations
M. S. G. has served as a speaker for Astellas. K. O. C. and K. A. M.: none to declare.

References
Association between IL28B gene polymorphisms and sustained virological response in patients coinfected with HCV and HIV in Brazil

Paulo Roberto Abrão Ferreira1,2, Carlos Santos3, Rodrigo Côrtes3, Alexandre Reis3, Simone de Barros Tenore1,2, Mariliza Henrique Silva2, Cintia Vilhena3 and Ricardo Sobhie Diaz1,3*

1Infectious Diseases Division, Paulista School of Medicine, Federal University of São Paulo, São Paulo, Brazil; 2Centro de Referência e Treinamento em DST-Aids de São Paulo, São Paulo, Brazil; 3Laboratório Centro de Genomas, São Paulo, Brazil

*Corresponding author. Retrovirology Laboratory, Federal University of São Paulo—EPM, R. Pedro de Toledo 781, São Paulo, SP 04039, Brazil. Tel: +55-11-9109-0445; Fax: +55-11-4192-3176; E-mail: rsdiaz@catg.com.br

Keywords: interferon, rs12979860, rs8099917


Sir,

The response of the hepatitis C virus (HCV) to pegylated interferon α treatment in association with ribavirin is variable and depends on virological and host characteristics. Genetic ancestry has been shown to be a factor in therapeutic progress. Patients of African-American and Amerindian descent typically show reduced sustained virological response (SVR) rates with pegylated interferon α and ribavirin compared with Caucasian patients.1,2 In contrast, Asian populations appear to have higher rates of SVR,3 which suggests an association between genetics and the development of SVR.

Recently, genome-wide association studies described several common and highly correlated single nucleotide polymorphisms (SNPs) in the vicinity of three interferon-λ genes, including IL28B, as being highly predictive of the response of HCV patients to treatment with pegylated interferon α and ribavirin, irrespective of the genotype involved.4,5 The same set of SNPs was subsequently associated with the natural elimination of HCV during the acute phase.6 This association was also demonstrated in HCV/HIV-coinfected patients.7 The Brazilian population conceivably consists of a mixture of people with Caucasian, African and Amerindian ancestries.8 Therefore, the present study assessed the association between IL28B gene polymorphisms and SVR in a cohort of HCV/HIV-coinfected Brazilian patients who were treated with pegylated interferon α and ribavirin.

All 26 of the HIV/HCV-coinfected patients that were included in this cohort were stable in relation to HIV infection. The patients received peginterferon alfa-2a (180 μg/week) or peginterferon alfa-2b (1.5 μg/kg/week) and ribavirin (15 mg/kg/day) for 48 weeks. Treatment compliance was assured in all cases. Patients who did not present undetectable HCV RNA by week 24 of treatment were considered non-responders and the medication was discontinued. The criterion for SVR was undetectable HCV RNA at 24 weeks after the end of treatment. The IL28B polymorphism was characterized by SNP analysis of the rs12979860 and rs8099917 regions by PCR, followed by restriction fragment length polymorphism (RFLP) analysis, as previously described,9 after the patients signed an Institutional Review Board (‘IRB’)-approved informed consent form. The results were subsequently confirmed by real-time quantitative PCR (qPCR) with molecular beacon analysis adapted according to the methodology described previously.4

Of the 26 patients, 15 were male and 10 presented with SVR. The average HCV nadir and pre-treatment CD4+ T cell counts were 326.5 and 625.6 cells/mm3, respectively. Twenty patients (76.9%) tested positive for HCV genotype 1 and six (23.1%) for genotype 3. The HCV RNA viral load was significantly higher in non-responders compared with responders (6.1 log10 versus 5.1 log10, Mann–Whitney P<0.031). The overall SVR rates for genotypes 1 and 3 were 25.0% and 83.3%, respectively (OR 3.33, 95% CI 1.44–7.71, P<0.010; for genotype 3) (Table 1).

The genotype frequencies for the IL28B SNP rs12979860 were CC=9 (34.6%), CT=13 (50.0%) and TT=4 (15.4%). The CC genotype was significantly associated with SVR (OR 4.40, 95% CI 1.49–13.03, P=0.003). The frequencies for the SNP rs8099917 were TT=14 (53.8%) and TG=12 (46.2%), with the TT genotype

Table 1. Univariate analysis of factors associated with SVR among HIV/HCV-coinfected individuals treated with pegylated interferon α and ribavirin

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
<th>Non-SVR (%)</th>
<th>SVR (%)</th>
<th>Comparison</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>&lt;40</td>
<td>5 (55.6)</td>
<td>4 (44.4)</td>
<td>&gt;40</td>
<td>1.24 (0.47–0.33)</td>
<td>0.648</td>
</tr>
<tr>
<td>IL28B rs12979860</td>
<td>CC</td>
<td>2 (22.2)</td>
<td>7 (77.8)</td>
<td>no CC</td>
<td>4.40 (1.49–13.03)</td>
<td>0.003</td>
</tr>
<tr>
<td>IL28B rs8099917</td>
<td>TT</td>
<td>7 (50.0)</td>
<td>7 (50.0)</td>
<td>no TT</td>
<td>3.00 (0.56–16.01)</td>
<td>0.191</td>
</tr>
<tr>
<td>HCV genotype</td>
<td>3</td>
<td>1 (16.7)</td>
<td>5 (83.3)</td>
<td>1</td>
<td>3.33 (1.44–7.71)</td>
<td>0.010</td>
</tr>
<tr>
<td>HCV RNA (IU/mL)</td>
<td>&lt;500000</td>
<td>1 (20.0)</td>
<td>4 (80.0)</td>
<td>&gt;500000</td>
<td>3.46 (1.17–10.25)</td>
<td>0.026</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>F1–2</td>
<td>11 (64.7)</td>
<td>6 (35.3)</td>
<td>F3–4</td>
<td>0.82 (0.28–2.40)</td>
<td>0.720</td>
</tr>
<tr>
<td>AIDS-defining illness</td>
<td>no</td>
<td>7 (58.3)</td>
<td>5 (41.7)</td>
<td>yes</td>
<td>1.16 (0.44–3.07)</td>
<td>0.756</td>
</tr>
<tr>
<td>Use of antiretrovirals</td>
<td>yes</td>
<td>15 (65.2)</td>
<td>8 (34.8)</td>
<td>no</td>
<td>1.91 (0.72–5.08)</td>
<td>0.286</td>
</tr>
</tbody>
</table>