The Effect of Transcatheter Arterial Chemoembolization on Hepatitis C Viremia

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Key Words. Hepatitis C • TACE • Hepatocellular carcinoma

Disclosures: Harrys A. Torres: Vertex, Novartis, Merck, Pfizer (CA); Merck, Genentech (RF). The other authors indicated no financial relationships.

(C/A) Consulting/advisory relationship; (RF) Research funding; (E) Employment; (H) Honoraria received; (OI) Ownership interests; (IP) Intellectual property rights/inventor/patent holder; (SAB) Scientific advisory board

To the Editor,

We read with great interest the article by Sansonno et al. [1] on transarterial chemoembolization (TACE) plus sorafenib in patients with hepatitis C virus (HCV)-related hepatocellular carcinoma (HCC). The authors did not provide information on the HCV kinetics of patients receiving this treatment intervention because of the oncologic nature of the study. Hepatitis B virus (HBV) and HCV viral reactivation are well-known complications of systemic chemotherapy [2, 3]. A few reports have evaluated changes in HBV viremia after TACE for HBV-associated HCC [4—6]. However, it is unknown whether or not TACE can induce HCV reactivation. Because of a lack of such information, we sought to determine the effect of TACE on HCV viremia in patients with HCV-associated HCC.

In this retrospective study, we analyzed the medical records of patients with both HCC and HCV infection seen at The University of Texas MD Anderson Cancer Center during January 2009 to December 2011. All patients had received at least one TACE session and had detectable HCV RNA in the serum within 6 months before and after TACE sessions. Patients who had received treatment for HCV infection were excluded. The study protocol was approved by the institutional review board. TACE sessions were performed as reported [7]. Because HCV RNA levels usually vary by ±0.5 log10 IU/mL [8], HCV reactivation was defined as an increase in HCV viral load ≥1 log10 IU/mL over baseline following TACE. Patients’ post-TACE HCV RNA and alanine aminotransferase (ALT) levels were compared with their pre-TACE levels using the Wilcoxon signed rank test.

We identified 11 patients with HCC and confirmed HCV infection with known pre- and post-TACE HCV RNA levels. Of these 11 patients, nine were men and six had genotype 1 infection. The median age was 55 years (range, 53—79 years). These patients underwent a total of 19 TACE sessions (mean, 1.7; range, 1—3), with pre- and post-TACE HCV RNA levels available for only 12 (63%) sessions. TACE was conducted with cisplatin (100 mg), mitomycin (10 mg), and doxorubicin (50 mg) for five sessions and doxorubicin drug-eluting beads (50 mg) for seven sessions. Viral loads were measured at a median of 60 days (range, 5—177 days) after TACE.

An increase in viral load (median, 0.29 IU/mL; range, 0.14—0.82 IU/mL) was observed after eight TACE sessions (Table 1; Fig. 1). Episodes of ALT elevation were noted after six of the 12 TACE sessions. None of the patients had received any other form of local or systemic therapy for HCC prior to TACE.

TACE leads to induction of hypoxia inducible factor 1α [9], a transcriptional regulator that might be involved in HCV replication [10]. However, we found that TACE did

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The Oncologist 2012;17:e21–e23 www.TheOncologist.com
not lead to HCV reactivation in chronically infected patients. Although there was an increase in ALT levels after some TACE sessions, it is unlikely that this was caused by a flare-up of chronic HCV infection because significant elevation of HCV RNA levels is a sine qua non condition for HCV reactivation [2].

In conclusion, this is the first report analyzing changes in HCV RNA levels after TACE for HCV-associated HCC. Because TACE did not lead to a substantial increase in HCV viral load, active chronic HCV infection should not contraindicate this procedure, and surveillance of HCV replication may not be necessary.

### Table 1. TACE sessions and changes in HCV RNA and ALT levels

<table>
<thead>
<tr>
<th>TACE no.</th>
<th>Agents used for TACE</th>
<th>HCV RNA level (log IU/mL)</th>
<th>ALT level (IU/mL)</th>
<th>HCV reactivation&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pre-TACE</td>
<td>Post-TACE</td>
<td>Change</td>
</tr>
<tr>
<td>1</td>
<td>Cisplatin, doxorubicin, mitomycin</td>
<td>6.01</td>
<td>6.39</td>
<td>+0.38</td>
</tr>
<tr>
<td>2</td>
<td>Cisplatin, doxorubicin, mitomycin</td>
<td>6.53</td>
<td>6.67</td>
<td>+0.14</td>
</tr>
<tr>
<td>3</td>
<td>Doxorubicin</td>
<td>4.58</td>
<td>4.38</td>
<td>−0.2</td>
</tr>
<tr>
<td>4</td>
<td>Doxorubicin</td>
<td>5.32</td>
<td>6.13</td>
<td>+0.81</td>
</tr>
<tr>
<td>5</td>
<td>Doxorubicin</td>
<td>6.13</td>
<td>5.84</td>
<td>−0.29</td>
</tr>
<tr>
<td>6</td>
<td>Cisplatin, doxorubicin, mitomycin</td>
<td>5.66</td>
<td>5.83</td>
<td>+0.17</td>
</tr>
<tr>
<td>7</td>
<td>Cisplatin, doxorubicin, mitomycin</td>
<td>5.9</td>
<td>6.72</td>
<td>+0.82</td>
</tr>
<tr>
<td>8</td>
<td>Doxorubicin</td>
<td>5.6</td>
<td>5.94</td>
<td>+0.34</td>
</tr>
<tr>
<td>9</td>
<td>Doxorubicin</td>
<td>5.99</td>
<td>5.3</td>
<td>−0.69</td>
</tr>
<tr>
<td>10</td>
<td>Cisplatin, doxorubicin, mitomycin</td>
<td>6.28</td>
<td>6.2</td>
<td>−0.08</td>
</tr>
<tr>
<td>11</td>
<td>Doxorubicin</td>
<td>6.48</td>
<td>6.73</td>
<td>+0.25</td>
</tr>
<tr>
<td>12</td>
<td>Doxorubicin</td>
<td>6.95</td>
<td>7.14</td>
<td>+0.19</td>
</tr>
</tbody>
</table>

Normal ALT values are in the range of 7–56 IU/mL.

<sup>a</sup>TACE number 4 and number 5 were performed on the same patient.

<sup>b</sup>Defined as an increase in HCV viral load ≥1 log IU/mL over baseline following TACE.

Abbreviations: ALT, alanine aminotransferase; HCV, hepatitis C virus; TACE, transcatheter arterial chemoembolization.

### Figure 1. HCV RNA levels before and after TACE procedure.

Displayed are box plots showing HCV RNA levels before and after TACE. No significant changes in HCV RNA after TACE were found.

Abbreviations: HCV, hepatitis C virus; TACE, transcatheter arterial chemoembolization.
AUTHOR CONTRIBUTIONS
Conception/design: Harrys A. Torres, Parag Mahale
Provision of study material or patients: Harrys A. Torres, Parag Mahale
Collection and/or assembly of data: Parag Mahale, Harrys A. Torres
Data analysis and interpretation: Parag Mahale, Harrys A. Torres
Manuscript writing: Parag Mahale, Harrys A. Torres
Final approval of manuscript: Parag Mahale, Ahmed Kaseb, Marta Davila, Harrys A. Torres

REFERENCES