In Defense of Hepatic Arterial Infusion for Hepatic Metastases of Colorectal Cancer

The recently published NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for the treatment of colorectal carcinoma are excellent and comprehensive, but I believe that one area deserves more comprehensive review: the use of hepatic arterial infusion (HAI) for the treatment of liver only metastases. I believe 3 circumstances exist in which HAI therapy may be considered. The first is after liver resection. Four randomized controlled trials address the use of HAI therapy after hepatic resection, and 3 of the 4 showed a significant increase in hepatic and overall disease-free survival (Table 1).2-6 The Memorial Sloan-Kettering Cancer Center (MSKCC) study randomized 156 patients after hepatic resection to continuous HAI of flouxuridine (FUDR) and dexamethasone (Dex) combined with systemic infusion of fluorouracil (5FU) and leucovorin (LV) versus systemic infusion of 5FU/LV alone for 6 months. Updated results after a median follow-up of 10 years reported survival rates of 41% and 27% at 10 years and progression-free-survivals of 31.3 and 17.2 months for the HAI + systemic infusion and systemic infusion alone groups, respectively (P = .02).3

An ECOG study randomized 100 patients to HAI FUDR + systemic 5FU infusion versus no further therapy after liver resection and showed an increase in progression-free survival. A randomized study of 122 patients from Greece reported a significant improvement in disease-free survival for HAI plus chemo-immunotherapy versus systemic infusion alone, although this was not seen in a German study that compared 5FU HAI administered through a port instead of a pump. House et al. evaluated patients who underwent liver resection between 2001 and 2005 and compared patients treated with HAI plus modern systemic chemotherapy versus systemic therapy alone. They reported improved survival (Figure 1) for those who received HAI.

HAI may also be considered as second-line therapy; studies show significant response rates and survival with this approach. In one study using HAI FUDR/Dex plus systemic oxaliplatin and irinotecan, the response rate in second-line therapy was 88% with a 35-month median survival. When compared with second-line systemic therapy, which has a low response rate and survival, HAI therapy seems to be superior and should be part of the treatment plan for patients with liver-only disease (Table 2).9-15

A third circumstance in which HAI should be considered is in the neoadjuvant (preoperative) setting to shrink hepatic metastases and make liver resection possible.

Table 1 Randomized Studies After Liver Resection: HAI + Systemic Infusion Versus Systemic Infusion Alone or Control

<table>
<thead>
<tr>
<th>Studies</th>
<th>#</th>
<th>HAI 2-Year (%)</th>
<th>Systemic infusion 2-Year (%)</th>
<th>HAI 5-Year (%)</th>
<th>Systemic Infusion 5-Year (%)</th>
<th>P Value</th>
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</thead>
<tbody>
<tr>
<td>MSKCC</td>
<td>156</td>
<td>55</td>
<td>45</td>
<td>40</td>
<td>30</td>
<td>0.02</td>
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<td>ECOG</td>
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<td>60</td>
<td>40</td>
<td>40</td>
<td>20*</td>
<td>0.03</td>
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<tr>
<td>Lorenz et al.</td>
<td>186</td>
<td>median</td>
<td>median</td>
<td>20</td>
<td>12.6*</td>
<td>NS</td>
</tr>
<tr>
<td>Lygidakis et al.</td>
<td>122</td>
<td>66</td>
<td>48</td>
<td>60</td>
<td>35</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

Abbreviations: HAI, hepatic arterial infusion; MSKCC, Memorial Sloan-Kettering Cancer Center; NS, not significant.

*No treatment in control arm.
In several systemic therapy–alone chemotherapy trials for patients with liver metastases that cannot be resected, the rate of conversion to resection is 15% to 30% in chemotherapy-naïve patients and less than 20% in previously treated patients. After concurrent neoadjuvant HAI and systemic therapy in a study of 49 patients, 57% of chemotherapy-naïve patients and 38% of previously treated patients were able to undergo resection. These data show the effectiveness of HAI therapy in patients with liver metastases, warranting broader consideration of this treatment option among certain patients with advanced colorectal cancer.

References


