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# What's Old Is New Again: Patients Receiving Hepatic Arterial Infusion Chemotherapy

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**H**epatocellular carcinoma (HCC) ranks as the eighth most common cancer in the world. Although uncommon in North America, the incidence of HCC in the United States has increased by 70% since the 1980s (Yu, Yuan, Govindarajan, & Ross, 2000). Estimates suggest that approximately 17,300 people in the United States will develop HCC in 2003 (Jemal et al., 2003). Generally, the most frequent causes of malignant hepatic disease in the United States are metastases from melanoma and primary tumors of the gastrointestinal tract, breast, and lung. Approximately 30% of patients with colorectal cancer present with liver involvement, and an additional 60% develop liver metastases (Kemeny, Kemeny, & Lawrence, 2000). The liver is the initial site of metastasis in 4% of breast cancers, 15% of lung cancers, and 24% of melanomas (Kemeny et al., 2000). Reviews of autopsy series

revealed that the prevalence of liver metastases was 70% in patients with melanoma, 45%–60% in those with breast carcinoma, and 30%–50% in those with lung carcinoma (Gilbert & Kagan, 1976; Weiss, Grundermann, & Torhorst, 1986).

The increased frequency of the liver as the initial site of metastasis is thought to be caused by the liver's large blood supply, which originates from the portal and systemic systems. Researchers have suggested that humoral factors that promote cell growth and cellular factors such as adhesion molecules favor metastatic spread to the liver (Kemperman, Driessens, La Riviere, Meijne, & Roos, 1995;

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**Key Words:** carcinoma, hepatocellular; neoplasm metastasis; infusions, intra-arterial

Long, Nip, & Brodt, 1994). Others speculate that the liver's geographic proximity to other intra-abdominal organs may facilitate malignant infiltration by direct extension (Bhattacharya, Rao, & Kowdley, 2002).

Surgical resection and systemic chemotherapy are standard treatments for hepatic disease. However, surgery is not an option for patients with advanced disease, and the response rate from systemic chemotherapy remains low (10%–30%) (Kemeny & Fata, 2001; Nagorney, van Heerden, Ilstrup, & Adson, 1989). An alternative therapy for patients with HCC or metastatic liver cancer is hepatic arterial infusion (HAI) chemother-

apy. HAI chemotherapy is the infusion of a chemotherapeutic drug through the hepatic artery directly into the liver.

HAI chemotherapy has been performed for more than 40 years as treatment for HCC and hepatic metastases. In the early 1970s and 1980s, approximately 375 patients were enrolled in randomized clinical trials comparing HAI therapy with systemic chemotherapy in the treatment of unresectable liver metastases from colorectal cancer (Venook & Warren, 2001). Researchers conducting early trials found response rates of more than 50% when compared to systemic therapy. However, HAI chemotherapy failed to show a survival advantage (Allen-Mersh, Earlam, Fordy, & Houghton, 1994; Chang et al., 1987; Hohn et al., 1989; Martin et al., 1990; Rougier et al., 1992). For example, Chang et al. randomized 64 patients to HAI of floxuridine (FUDR) versus

systemic FUDR and observed response rates of 62% in the HAI group and 17% in the systemic group. Two-year survivals were not statistically significant (22% and 15%, respectively). Another randomized trial conducted by Martin et al. reported a response

*Submitted May 2003. Accepted for publication June 17, 2003. (Mention of specific products and opinions related to those products do not indicate or imply endorsement by the Clinical Journal of Oncology Nursing or the Oncology Nursing Society.)*

Digital Object Identifier: 10.1188/03.CJON.647-652