From the Editor

Technological and Clinical Advances in Liver-Directed Therapy for Hepatocellular Carcinoma

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We tend to think of the main therapeutic disciplines in cancer as being related to surgical, medical, and radiation therapies. However, the management of hepatocellular carcinoma (HCC) relies heavily on the discipline of interventional radiology (IR) for both imaging and liver-directed therapies. As such, the update in this issue of *The American Journal of Hematology/Oncology®* on IR-based therapies for HCC is a valuable review for our readership. The incidence of HCC is rising due to both viral and obesity-related inflammation/cirrhosis, and it is a more common cancer in countries where vertical transmission of hepatitis is prevalent.[1] A majority of HCC cases are not resectable and generally not curable. Systemic chemotherapy is largely ineffective, and kinase inhibitor therapy trials with sorafenib and, more recently, regorafenib have shown activity and survival improvements, but these agents do not provide long-term control.[2,3] There is a long history of locally directed therapy, which is facilitated by the fact that the liver has dual circulation through the hepatic arteries and veins, allowing for the arterial delivery of chemotherapy and radiotherapy with or without embolization, and even greater selectivity as tumors are primarily vascularized from arteries. Given the fact that liver-directed therapies can arrest growth of specific lesions that may be symptomatic, it has been difficult to design and conduct randomized trials compared with no treatment or systemic therapy only.

This review by Windham-Herman and colleagues highlights improvements in imaging and delivery, the chemotherapeutic and radioactive agents, and key trials that may help the clinician integrate this modality. Additionally, some of the theoretical considerations and individual trial results may help provide a basis for the clinical situation and timing for referral of such interventions. It is important to recognize that in most cases, the use of intra-arterial therapy is palliative, can achieve responses, and can delay clinical deterioration. In some cases, survival advantages from randomized trials can help point to the specific technique that may be recommended.[4] This article should serve to remind us that the modern interdisciplinary team for the management of HCC should clearly involve interventional/therapeutic radiology.

References

1. Ghouri YA, Mian I, Rowe JH. Review of hepatocellular carcinoma: epidemiology, etiology, and carcinogenesis. *J Carcinog.* 2017;16:1. doi: 10.4103/jcar.JCar_9_16.
2. Llovet JM, Ricci S, Mazzaferro V, et al; SHARP Investigators Study Group. Sorafenib in advanced hepatocellular carcinoma. *N Engl J Med.* 2008;359(4):378-390. doi: 10.1056/NEJMoa0708857.
3. Bruix J, Qin S, Merle P, et al; RESORCE Investigators. Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): a randomised, double-blind, placebo-controlled, phase 3 trial [published correction appears in *Lancet.* 2017;389(10064):36]. *Lancet.* 2017;389(10064):56-66. doi: 10.1016/S0140-6736(16)32453-9.
4. Katsanos K, Kitrou P, Spiliopoulos S, et al. Comparative effectiveness of different transarterial embolization therapies alone or in combination with local ablative or adjuvant systemic treatments for unresectable hepatocellular carcinoma: a network meta-analysis of randomized controlled trials. *PLoS One.* 2017;12(9):e0184597. doi: 10.1371/journal.pone. 0184597.