Epithelial carcinoma (HCC) is one of the most common cancers in Taiwan and in the world. The overall prognosis of HCC is very poor. Surgical resection is the only potentially curative treatment for HCC and is most effective for small tumors. Unfortunately, many HCC patients have tumor recurrence after surgery and most patients are not eligible for surgery because of advanced stage and/or underlying compromised hepatic reserve at presentation.

Liver transplantation is another treatment option, but potential recipients far outnumber donors worldwide. Alternative non-surgical methods include transcatheter arterial chemoembolization (TACE) and percutaneous ultrasound-guided intratumoral injection of cell-killing agents such as pure ethanol and acetic acid, as well as radio-frequency thermal ablation. Other treatments, such as radiotherapy or chemotherapy, are ineffective, and the results unsatisfactory. In addition, some HCC patients with poor liver reserve, bulky tumors, major vessel thrombosis, multiple tumors involving both lobes of the liver, or distant metastasis are not good candidates for these treatments. New, effective, and less toxic methods are urgently needed.

Intraarterial chemotherapy (IAIC), first reported by Klopp et al., has the advantage of increasing the concentration of chemotherapeutic agents locally into the tumor with fewer systemic side effects than that seen with systemic chemotherapy. Several studies have demonstrated modest benefits both in terms of tumor responses and survival, but there was no consensus regarding the most effective regimen or the best route of administration.

In this issue, Lin et al. reported that continuous intraarterial infusion chemotherapy with cisplatin, mitomycin-C, leucovorin, and 5-fluorouracil is effective with tolerable side effects for patients with advanced HCC who were not eligible for surgical resection or other local treatments. A response rate of 28.3% and an overall survival of 13.2 months are promising, compared with previous IAIC studies and systemic chemotherapy. The major drawback of the clinical study is that one third of the enrolled patients (25 out of 78 patients) were excluded from the analysis. Four patients died within 1 month after IAIC and 21 patients either refused further treatment or had their treatment stopped because of cirrhotic complications. The withdrawal of these 25 patients may in part be due to the side effects of the IAIC. The high patient drop-out rate of 25 in 78 (32%) in this study of IAIC treatment should be considered a serious problem. Exclusion of these patients from the total number enrolled could result in overestimation of survival and underestimation of the adverse effects of IAIC. Those patients whose disease progressed during or after the first course of IAIC are better included so that response and toxicities can be better evaluated and analysis by the intent-to-treat method can more exactly reflect the results of IAIC in these HCC patients.

Eleven patients underwent additional local therapies (TAE in 10 patients and percutaneous acetic acid injection in 1 patient) and they got promising responses following these additional local therapies in the report by Lin et al. These treatments may in part account for the good survival in this study. Multi-modality treatment may benefit many HCC patients and be a future trend in HCC treatment.

In this issue, Lin et al. found that absence of main vessel thrombosis and alpha-fetoprotein (AFP) reduction percentage > 50% following treatment were significant predictors for tumor response. AFP reduction > 50% following treatment per se is a tumor response marker.
 Obviously, such tumor response markers are predictors of the tumor response, but their consideration in an analysis of tumor response predictors is inappropriate.

 IAIC, unlike TACE or percutaneous ethanol/acetic acid injection therapy, might have systemic effects. However, IAIC does not seem to have a great impact on the tumor thrombus obstruction in major vessels, since IAIC did not change the poor prognosis stemming from major vessel thrombosis. Other more effective modalities are needed to treat such patients.

 Although one third of patients were excluded from the analysis, Lin et al.\textsuperscript{9} still demonstrated some palliative effects with mild side effects in patients with advanced HCC, as did other previous studies. Since the general condition of advanced HCC patients frequently is generally poor, some signs and symptoms of discomfort are inevitable during the course of treatment. Although IAIC may have some palliative effect in prolonging survival and improving the quality of life, only 1 controlled study demonstrated the rate of response and performance status improvement was higher in patients treated with IAIC than with systemic chemotherapy.\textsuperscript{10} There was no difference in survival between the 2 groups in that study. No other controlled trials demonstrate definitely its superiority to conventional systemic chemotherapy in advanced HCC patients till now. Whether IAIC can be another choice for unresectable advanced HCC depends on the results of further larger controlled studies.

REFERENCES