

The evolving treatment landscape of hepatocellular carcinoma: more choices, more responsibility

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Hepatocellular carcinoma (HCC) is the 4th most common cause of cancer-related deaths worldwide¹. The coexistence of HCC and liver cirrhosis often poses a unique challenge in identifying the optimal treatment approach in the context of preserving hepatic function. As a consequence, multidisciplinary care has been the cornerstone of HCC management—considering liver morphology and function, tumour biology, and the patient's status. With insights from internationally recognized guest contributors, this special *Current Oncology* supplement highlights the current state of the art in the clinical management of HCC, recognizing the rapidly changing landscape of treatment options.

In their review of the epidemiology and screening for HCC, Frager and Schwartz² (Albert Einstein College of Medicine, NY, U.S.A.) highlight trends in the global incidence and prevalence of HCC and present current recommendations for HCC surveillance and screening. They also highlight metrics for ascertainment of hepatic reserve and discuss the critical role of those metrics in HCC treatment decision-making.

Therapeutically, locoregional therapies have always played an important role in HCC management. In this supplement, Cardarelli-Leite *et al.*³ (BC Cancer–University of British Columbia, Vancouver, BC) elegantly review the expanding options for locoregional therapy in intermediate-stage HCC, either sequentially or potentially in combination with systemic therapies. They also discuss the complexities of balancing tumour biology, tumour and hepatic morphology, and hepatic functional reserve within the context of a multidisciplinary assessment.

For patients with advanced HCC (Barcelona Clinic Liver Cancer stage C), the systemic therapy landscape has changed considerably. After the publication of the practice-changing SHARP trial more than 12 years ago demonstrated the role of the multikinase inhibitor sorafenib in the first-line treatment of HCC⁴, the oncology community has witnessed the recent emergence of positive phase III trials demonstrating the utility of lenvatinib, regorafenib, and cabozantinib in the first- and second-line settings. Perera *et al.*⁵ (Princess Margaret Cancer Centre, Toronto, ON) comprehensively review the evidence supporting the role of lenvatinib and sorafenib in

the first-line setting and address factors that might influence the choice of therapy. They also discuss the importance of timely commencement of systemic therapy, including the appropriate identification of patients who might no longer be benefitting from continued liver-directed therapies such as transarterial chemoembolization.

With the publication this year of the first positive phase III trial demonstrating a survival benefit with immunotherapy in untreated advanced HCC⁶, the combination of the PD-L1 inhibitor atezolizumab and the vascular endothelial growth factor inhibitor bevacizumab has emerged as a first-line treatment option. There is now intense interest in the role of immunotherapy combinatorial approaches for patients with untreated advanced HCC, and multiple phase III trials are well underway. Weinmann and Galle⁷ (Mainz University Hospital, Germany) provide an excellent review of the clinical evidence for immunotherapy in HCC in the upfront and pretreated settings. They also discuss the relevant factors that clinicians must consider in terms of optimal patient selection and safety.

Finally, with sorafenib no longer the only first-line systemic therapy option for advanced HCC, the availability of alternative first-line options presents challenges in determining the preferred post-progression sequencing strategy. In their review, Amaro and Tam⁸ (Tom Baker Cancer Centre, Calgary, AB) present the clinical evidence supporting the efficacy of post-progression therapies in HCC and offer valuable insights into potential sequencing algorithms that reflect contemporary practices.

The future seems bright, with hope for improving outcomes for patients with HCC. For those of us involved in the management of HCC, the emergence of more efficacious therapeutic options is long overdue and most welcome. Nonetheless, uncertainties remain. More options inevitably lead to more questions and greater responsibility for an appropriate treatment selection. Now, the oncology community must work toward defining optimal management strategies and sequences that will afford patients the best outcomes, while still balancing disease biology with hepatic reserve—all fundamentally underpinned by a multidisciplinary care approach.

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CONFLICT OF INTEREST DISCLOSURES

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