



# Regional differences: clinical practice guidelines on the management of hepatocellular carcinoma

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Hepatocellular carcinoma (HCC) remains a global health burden, stimulating the scientific community to further deepen their research in this field. In order to successfully translate novel insights into clinical practice and provide clinicians with evidence-based care for their patients, HCC clinical practice guidelines were published and need to be updated periodically.

China has a plethora of patients who suffer from HCC. However, in contrast to Western countries, the underlying disease in Chinese HCC patients is mainly hepatitis B. This considerable difference may well influence diagnostics and efficacy of treatments, particularly systemic therapy. Thus, it is reasonable for the Chinese hepatology community to update their HCC clinical guidelines independently from Western hepatology societies such as EASL or AASLD. However, their comparison is certainly stimulating to the scientific discussion. Therefore, Xie *et al.* just published such a nice comparison of the latest update of the Chinese guidelines published in 2019 to recommendations from EASL and AASLD (1).

While sharing many similarities, the etiological and thus molecular differences lead to clearly distinct recommendation for the use of the tumor marker AFP for HCC surveillance and may also influence selection of systemic therapy options.

In contrast to EASL not recommending AFP for surveillance due to false positive screening and cost-effectiveness calculations, the Chinese guidelines

recommend AFP. Xie *et al.* point out that HBV-related HCCs tend to have higher AFP levels compared to HCC due to other causes (1). Although this may be the case, solid data supporting AFP efficacy particularly in HBV-related HCC is lacking. The reference to the work by Tayob *et al.* retrospectively investigating AFP sensitivity in the HALT-C trial population certainly need further confirmation as these patients suffered from hepatitis C (2). Just recently novel trials investigating AFP, AFP-L3, DCP and the GALAD score (3,4) as the most prominent tumor markers for HCC were reported to perform unsatisfactory at the AASLD annual meeting. The GALAD score, which performed best in terms of detection rate was demonstrated to be associated with a high false positive prediction rate of over 20% (5). Thus, the debate about the use of AFP and other biomarkers for surveillance and early detection of HCC remains challenging and may not only be a matter of different etiologies or ethnic background among Chinese and Western patients.

Furthermore, the landscape of systemic therapy has significantly changed over the past two years. With the results from the IMbrave150 trial being reported at 2019 ESMO Asia, systemic treatment of HCC has entered a new level. Combination of atezolizumab and bevacizumab yielded a significantly improved overall survival in comparison to sorafenib treatment (6). However, subgroup analysis demonstrated best efficacy of this immunotherapy in patients with viral hepatitis, which may be particularly

interesting in China. With additional companies releasing press notes on the efficacy of durvalumab and tremelimumab in the HIMALAYA phase III trial (7) and atezolizumab and cabozantinib in COSMIC-312 phase III trial (8) we are certainly at the beginning of a new era. Therefore the future development of the Chinese PD-1 inhibitor camrelizumab will also be of great interest. Given these recent developments, the role of TKIs such as lenvatinib or sorafenib will have to be re-defined, just as the role of former second-line therapeutics, such as cabozantinib, ramucirumab, or regorafenib.

Overall, many common paradigms regarding surveillance, diagnosis, and treatment are shared among the Chinese and Western recommendations. However, a few differences remain. Given the etiological and ethnic differences, joint efforts and clinical trials would be extremely valuable to further improve HCC diagnostics and treatment. The elaborate summary by Xie *et al.* is certainly a valuable initiative to foster joint efforts to fight HCC.

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