LV DB 1

Updated guidelines for BCLC stage B / modified UICC / Korean guidelines - classification and Tx

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Lecture : In general, the intermediate stage of hepatocellular carcinoma (HCC) is defined as multifocal HCC (beyond Barcelona Clinic Liver Cancer [BCLC]-A criteria) with preserved liver function, no cancer-related symptoms, and no vascular invasion or extrahepatic spread. However, HCC in the intermediate stage is heterogeneous in terms of tumor burden (size, shape and number) and prognosis is also influenced by the levels of tumor marker (namely AFP) and the degree of liver function impairment (even within Child-Pugh class A). Although robust cut-offs are not available, AFP or hepatic functional reserve can affect the overall outcome of the intermediate stage HCC.

Recently, there have been the major updates on the recommendations of treatment for the intermediate stage. The updated 2022 BCLC version stratifies the intermediate stage into three subcategories according to tumor burden and liver function. The first subgroup within BCLC-B includes patients with well-defined HCC nodules. These patients could be candidates for LT if they meet the 'Extended Liver Transplant (LT) criteria' according to the criteria, in which the decision-making could be based on AFP and DCP cutoffs (eg, <400 and <7.5 ng/mL, respectively), 18F-FDG PET nonavid tumor, and if applicable, response to loco-regional therapy to ensure acceptable tumor biology. However, acceptance of the expanded LT criteria should be weighed by the potential for higher recurrence and lower long-term survival. Thus, several groups have established a concentration limit beyond which LT is not considered. A 1,000 ng/dl cut-off value is currently applied as an exclusion criterion. While downstaging therapy may induce a reduction of AFP, there are no robust data to define the magnitude and/or duration of reduction required before considering LT.

The second subgroup comprises patients without the option of LT but who have preserved portal flow and defined tumor burden, suggesting the feasibility of selective access to feeding tumor arteries. They are candidates for transarterial chemo-embolization (TACE). The third subgroup includes patients who neither meet the 'Extended LT criteria' nor the TACE criteria to secure optimal outcomes. Systemic therapy should be considered for these patients. This subgroup within BCLC-B includes patients with diffuse, infiltrative, extensive HCC liver involvement. They do not benefit from TACE, and systemic therapy should be the recommended option, although there is no strict cut-off for when this is the case.

The updated 2022 KLCA-NCC Korean practice guidelines for the management of HCC provide the best and alternative treatments according to the modified UICC (mUICC) staging system which has been adopted as a primary staging system for HCC in 2003. According to the updated Korean guidelines, the best option for multifocal HCCs (beyond Milan) > 3 cm without vascular invasion is conventional TACE (cTACE) (A), while alternative treatments include resection, transarterial radioembolization (TARE), and external bead radiotherapy (EBRT), which can be opted according to tumor burden and reserved liver function. For the subgroup with multifocal HCCs ≤ 2 cm with vascular invasion, the best treatments include the 1st-line systemic therapy (A), cTACE+EBRT (B), and cTACE (Vp1-2) (B). Patients who have multifocal HCCs > 2 cm with vascular invasion are best candidates for the 1st-line systemic therapy (A) and cTACE+EBRT (B). Alternative treatments for this subgroup include cTACE and HAIC (hepatic arterial infusion chemotherapy).

Tumor burden such as size, number, and morphology as well as liver function are heterogeneous in the intermediate stage HCC. The initial recommendations in the guidelines are based on robust scientific evidence, but the clinical decision-making section highlights the complexity of management at the individual level and the need to personalize decisions according to a multiparametric assessment by multidisciplinary team approaches, which are highly expected to improve the overall outcomes of patients in this stage.