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Hepatocellular Carcinoma: Molecular Biology and Therapy

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Hepatocellular carcinoma (HCC) is one of the most common malignancies worldwide. Advanced and metastatic HCC remain very challenging to treat mainly because of two factors: (1) the hostile environment of the liver with HCC and myriad drug-resistance genes that render chemotherapy relatively ineffective; and (2) the often underlying cirrhotic condition of the liver, which necessitates lower chemotherapy doses to mitigate toxicity.

The presence of cirrhosis is an important factor that needs to be assessed when evaluating any patient with HCC. A scoring system, when used in the appropriate patient population (eg, CLIP for hepatitis C, and CUPI for hepatitis B), should provide the medical oncologist with an objective prediction of the likely overall survival and might assist in the selection of an optimal treatment approach.

Almost all classes of chemotherapeutic single agents and a variety of combinations have been tested in HCC; however, none has demonstrated substantial activity or a clear survival benefit.

In recent years, there has been better understanding of the molecular events that lead to HCC oncogenesis. In parallel, multiple novel therapeutic agents are being assessed in HCC. In addition to angiogenesis, several potential targets are evident along the signal transduction pathway. Thus far, no single molecular targeted therapy has succeeded in becoming a standard of care for advanced HCC. It is imperative to continue investigating this approach, as it will help us acquire a better understanding of HCC pathogenesis, and ultimately find a treatment for advanced-stage disease.