Section 5

New directions

A series of both scientific and clinical advances is changing the management of hepatocellular carcinoma (HCC). These include:

1. The identification of preventable and treatable causal factors, including hepatitis B (HBV), hepatitis C (HCV), alcoholism, and obesity (non-alcoholic steatotic hepatitis [NASH]).
2. The characterization of molecular and proteomic profiles for HCC prognosis, disease subtyping, and rational drug selection.
3. The identification of circulating tumor cells for non-invasive molecular typing.
4. The identification of tumor stem/progenitor cell characteristics for HCC subtyping and as treatment targets.
5. The development of large numbers of multikinase inhibitors that are currently undergoing clinical trial assessment and comparison. In particular, a randomized controlled Phase II trial in patients with HCC on second-line therapy showed that tivantinib (ARQ 197), a specific inhibitor of Met oncogene, had increased overall survival in that subset of patients with tumors having high levels of its Met target.
6. An array of newer therapies of different drug classes aimed at a wide range of targets in cell growth, apoptosis, autophagy, and tumor invasion pathways.
7. Newer regional chemotherapy and radiotherapy regimens and delivery systems.
8. The extension of liver transplantation to larger HCCs and its wider availability through use of living-related organ donors; the development of a more flexible liver transplantation patient selection process. For example, the Metroticket model aims to survey patients transplanted outside of the Milan criteria, and to also provide a prognostic calculator to give physicians and their patients an estimated survival prediction after liver transplantation.
9. New radiological techniques to assess the changes in HCC vascularity associated with angiogenic drug actions.
10. Re-evaluation of the use of tumor biopsy to obtain molecular signatures.
11. Recognition of the importance of non-tumor liver parenchyma (microenvironment) for tumor growth control and as a source of prognostic profiling in patients with HCC.
12. The evaluation of kinase and other inhibitors in neo-adjuvant and adjuvant therapy associated with resection, liver transplant, and minimization of transplant waiting list drop-out; identification of use of a vitamin A analog as adjuvant therapy (peretinoin, NIK-333).
13. Re-evaluation of the role or limitation of tumor responses, as kinase inhibitors can enhance survival without HCC size responses.
14. The development of combination therapies to enhance tumor control rates, by either using molecularly targeted drugs that inhibit differing growth pathways, or kinase inhibitors combined with either chemoembolization drugs or radioembolization with ^{90}Yttrium.
15. Realization of the antitumor role of HBV and HCV treatment in patients diagnosed with HCC.

B. I. Carr, *Understanding Liver Cancer*, DOI: 10.1007/978-1-910315-02-6_5,

Summary for patients, families, and caregivers

There has been much improvement in the understanding of what causes HCC as well as its underlying biology. This has led to the refinement and development of new prevention, management, and treatment options for patients with the disease. Medical research will continue to advance our knowledge of HCC and enable further treatment choices for patients with this complex disease.

Further reading

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