Hepatocellular Carcinoma

Cancer Centre of Southeastern Ontario
Standard Management Guidelines

Intended for use by Clinicians and Health Care Providers involved in the Management or Referral of adult patients with hepatocellular carcinoma (HCC)

Section	Activity	Activity Description	Details	Reference(s)
AA	Cancer Centre Referrals		• All new suspected HCC in patients with cirrhosis should be referred to Liver Clinic (Hepatologist) • In the absence of cirrhosis, patients should be referred to Hepatobiliary surgery • Patients who have been reviewed by HCC MCC and thought to be potential candidates for systemic therapy and/or radiation could be referred to CCSEO	

A	Diagnosis		• Diagnosis can be made by :
			  • Characteristic imaging (liver protocol CT or MRI)
			  • Biopsy may occasionally be required after discussion at HCC MCC
				[1]

B	History and Physical Exam		• History: hepatitis C and B infection and risk factors for infection, alcohol use, personal or family history of hemochromatosis, Non-alcoholic fatty liver disease (NFLD and NASH), α-1-antitrypsin deficiency • History of cirrhosis, hepatic encephalopathy, esophageal varices, jaundice and ascites • Performance status • Stigmata of cirrhosis, chronic liver disease and portal hypertension	
C	Investigations		• Labs: CBC with diff, LFTs, albumin, PT/INR, AFP, creatinine and electrolytes. Use labs to risk stratify based on Child's score and MELD score. • Hep B SAg, Hep C Ab (diagnosis of chronic infection)	

Section	Activity	Activity Description	Details	Reference(s)
			• Imaging (liver protocol CT or MRI) • CT chest	

D	Pathology of diagnostic biopsy and /or resection	Pathology guidelines (includes Synoptic report)	• Pathology may not always be required
			• KGH pathology review of all cases with outside pathology
			• Biopsy specimen:
			  • surgical report to include – tumour type (histology), grade, vascular invasion, degree of liver fibrosis/cirrhosis
			• Resection specimen:
			  • surgical report to include – location of primary tumor, tumour type (histology), grade, size, presence of lymphovascular and/or perineural invasion, assessment of resection margins, degree of liver fibrosis/cirrhosis in non-tumorous liver	

E	Post-Investigation Management	Curative intent	• Surgical resection first line treatment for patients who can tolerate resection (i.e. well compensated cirrhosis with low-moderate portal HTN) • Ablation can be considered curative for lesions up to 3 cm • Transplantation is reserved for multifocal HCC or advanced cirrhosis that precludes liver resection. However, must meet local transplant criteria. Any radiographic evidence of vascular invasion or extra-hepatic disease precludes transplantation. Bridging therapy should be considered in discussion with transplant center • There is no role for adjuvant sorafenib after resection or ablation	[2] [3] [4]

Section	Activity	Activity Description	Details	Reference(s)
		Advanced disease	• Liver directed therapy. This may include TACE, TAEE or bland embolization. May not be an option in the setting of frank vascular invasion • Sorafenib in patients who have failed TACE or who are not candidates for TACE, and who have good performance status and CHILD class A • Second line Regorafenib • Role of SBRT • Best supportive care • Clinical trial	[5], [6] [7]
		Locally recurrent disease	• Depends on initial management and presence or absence of cirrhosis. • Recurrent disease can still be treated with curative intent – resection, transplantation, RFA. • Sorafenib • SBRT • Clinical trial (if available)	
F	Follow-up with no		• Follow up in Liver Clinic or by Hepatobiliary surgeons	

Section	Activity	Activity Description	Details	Reference(s)
	Evidence of Disease		• Liver imaging q3-4 months for 2 years; q 6 monthly depending on presence/absence of cirrhosis and underlying comorbidities • Serial AFP's can be considered if elevated at baseline	
G	Controversies		• Role of Sorafenib in patients with good performance status who CHILD class B. • Role of TACE in metastatic disease.	
H	Clinical Trials		• https://intraprod.kgh.on.ca/cct/full-protocol-list	

References

1. Bruix, J., & Sherman, M. (2011). AASLD Practice Guideline Management of Hepatocellular Carcinoma: An Update. *Hepatology*, Vol 53, 1020-1022. [back]
https://www.aasld.org/sites/default/files/guideline_documents/HCCUpdate2010.pdf

2. Bruix, J. et al. (2015). Adjuvant sorafenib for hepatocellular carcinoma after resection or ablation (STORM): a phase 3, randomised, double-bline, placebo-controlled trial. *The Lancet Oncology, Volume 16, Issue 13*, 1344-1354. [back]
http://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(15)00198-9/abstract

3. Baldassarre, F., Baerlocher, M., & Dawson, L. (2014). Focal Tumour ablation: thermal ablation of hepatocellular carcinoma and metastases from colorectal carcinoma: evidence summary. *Cancer Care Ontario* [Internet]. [back]
https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=332299

4. Trillium Gift of Life Network: Ontario's Adult Referral and Listing Criteria for Liver/Liver-Bowel Transplantation V. 2.0. [back]
https://www.giftoflife.on.ca/resources/pdf/5_Adult_Liver_Liver-Bowel_Tx_Referl_Listng_Criteria_1030.pdf

5. Llovet, J., Ricci, S., Mazzaferro, V., Hilgard, P., Gane, E., Blanc, J.-F., et al. (2008). Sorafenib in advanced hepatocellular carcinoma. *New England Journal of Medicine*, 359: 378-390. [back]
http://www.nejm.org/doi/pdf/10.1056/NEJMoa0708857

6. Cheng, A., YK, K., Chen, Z., Tsao, C., Qin, S., Kim, J., et al. (2009). Efficacy and safety of sorafenib in patients in the Asia-Pacific region with advanced hepatocellular carcinoma: a phase III randomised, double-blind, placebo-controlled trial. *The Lancet Oncology*, 10(1):25-34. [back]
http://www.thelancet.com/pdfs/journals/lanonc/PIIS1470-2045(08)70285-7.pdf

7. Bruix, J., Qin, S., Merle, P., Granito, A., Huang, Y., Bodoky, G., et al. (2017). Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): a randomised, double-blind, placebo-controlled, phase 3 trial. *The Lancet*, 389(10064):56-66. [back]
http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(16)32453-9/abstract

Revisions