

## ***Recent Advances in the Management of Patients with Advanced Hepatocellular Carcinoma: How Does Your Approach Compare with the Experts’?***

### **TOOLKIT**

Resources	Address
Abou-Alfa GK, et al. A randomized, multicenter phase 3 study of durvalumab (D) and tremelimumab (T) as first-line treatment in patients with unresectable hepatocellular carcinoma (HCC): HIMALAYA study. <i>J Clin Oncol.</i> 2018;36(suppl; abstr TPS4144).	<a href="https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01789128/full">https://www.cochranelibrary.com/central/doi/10.1002/central/CN-01789128/full</a>
Abou-Alfa GK, et al. Cabozantinib in patients with advanced and progressing hepatocellular Carcinoma. <i>N Engl J Med.</i> 2018; 379(1):54-63.	<a href="https://www.nejm.org/doi/full/10.1056/nejmoa1717002">https://www.nejm.org/doi/full/10.1056/nejmoa1717002</a>
Abu-Sbeih H, et al. Clinically significant hepatotoxicity due to immune checkpoint inhibitors is rare but leads to treatment discontinuation in a high proportion. <i>Hepatology.</i> 2018;68(suppl 1):25A-26A.	<a href="https://aasldpubs.onlinelibrary.wiley.com/doi/epdf/10.1002/hep.30256">https://aasldpubs.onlinelibrary.wiley.com/doi/epdf/10.1002/hep.30256</a>
American Cancer Society (ACS). Cancer Facts & Figures 2019.	<a href="https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf">https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf</a>
Atezolizumab (Tecentriq®) PI 2020	<a href="https://www.gene.com/download/pdf/tecentriq_prescribing.pdf">https://www.gene.com/download/pdf/tecentriq_prescribing.pdf</a>
Berhane S, et al. Role of the GALAD and BALAD-2 serologic models in diagnosis of hepatocellular carcinoma and prediction of survival in patients. <i>Clin Gastroenterol Hepatol.</i> 2016;14(6):875-886.e6.	<a href="https://pubmed.ncbi.nlm.nih.gov/26775025/">https://pubmed.ncbi.nlm.nih.gov/26775025/</a>
Bevacizumab (Avastin®) PI 2021.	<a href="https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/125085s0169lbl.pdf">https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/125085s0169lbl.pdf</a>
Brahmer JR, et al. Management of immune-related adverse events in patients treated with immune checkpoint inhibitor therapy: American Society of Clinical Oncology Clinical Practice Guideline. <i>J Clin Oncol.</i> 2018;36(17):1714-1768.	<a href="https://pubmed.ncbi.nlm.nih.gov/29442540/">https://pubmed.ncbi.nlm.nih.gov/29442540/</a>
Colevas AD, Setser A. The NCI Common Terminology Criteria for Adverse Events (CTCAE) v 3.0 is the new standard for oncology clinical trials. <i>J Clin Oncol.</i> 2004;22(14 suppl):6098.	<a href="https://ascopubs.org/doi/abs/10.1200/jco.2004.22.90140.6098">https://ascopubs.org/doi/abs/10.1200/jco.2004.22.90140.6098</a>
CT/MRI LI-RADS v2018 CORE.	<a href="http://www.acr.org/-/media/ACR/Files/RADS/LI-RADS/LI-RADS-2018-Core.pdf?la=en">www.acr.org/-/media/ACR/Files/RADS/LI-RADS/LI-RADS-2018-Core.pdf?la=en</a>
De Martin E, et al. Characterization of liver injury induced by cancer immunotherapy using immune checkpoint inhibitors. <i>J Hepatol.</i> 2018;68(6):1181-1190.	<a href="https://pubmed.ncbi.nlm.nih.gov/29427729/">https://pubmed.ncbi.nlm.nih.gov/29427729/</a>
El-Khoueiry AB, et al. Impact of antitumor activity on survival outcomes, and nonconventional benefit, with nivolumab (NIVO)	<a href="https://ascopubs.org/doi/abs/10.1200/JCO.2018.36.4_suppl.475">https://ascopubs.org/doi/abs/10.1200/JCO.2018.36.4_suppl.475</a>

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El-Khoueiry AB, et al. Nivolumab (NIVO) plus ipilimumab (IPI) combination therapy in patients (Pts) with advanced hepatocellular carcinoma (aHCC): Long-term results from CheckMate 040. <i>J Clin Oncol.</i> 2021;39(3_suppl):269-269.	<a href="https://ascopubs.org/doi/abs/10.1200/JCO.2021.39.3_suppl.269">https://ascopubs.org/doi/abs/10.1200/JCO.2021.39.3_suppl.269</a>
European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. <i>J Hepatol.</i> 2018;69(1):182-236.	<a href="https://pubmed.ncbi.nlm.nih.gov/29628281/">https://pubmed.ncbi.nlm.nih.gov/29628281/</a>
Finn R, et al. IMbrave150: updated overall survival (OS) data from a global, randomized, open-label Phase III study of atezolizumab (atezo) + bevacizumab (bev) vs sorafenib (sor) in patients (pts) with unresectable hepatocellular carcinoma (HCC). <i>Liver Cancer Summit.</i> 2021. Abstract 005.	<a href="https://easl.eu/wp-content/uploads/2021/01/Digital-Liver-Cancer-Summit-2021-Abstract-book.pdf">https://easl.eu/wp-content/uploads/2021/01/Digital-Liver-Cancer-Summit-2021-Abstract-book.pdf</a>
Finn RS, et al. Mbrave150: Updated efficacy and safety by risk status in patients (pts) receiving atezolizumab (atezo) + bevacizumab (bev) vs sorafenib (sor) as first-line treatment for unresectable hepatocellular carcinoma (HCC) <i>Cancer Res.</i> 2021;81(13_Suppl):Abstract nr CT009;	<a href="https://cancerres.aacrjournals.org/content/81/13_Supplement/CT009">https://cancerres.aacrjournals.org/content/81/13_Supplement/CT009</a>
Finn RS, et al. Outcomes of sequential treatment with sorafenib followed by regorafenib for HCC: Additional analyses from the phase III RESORCE trial. <i>J Hepatol.</i> 2018;69(2):353-358. doi:10.1016/j.jhep.2018.04.010	<a href="https://pubmed.ncbi.nlm.nih.gov/29704513/">https://pubmed.ncbi.nlm.nih.gov/29704513/</a>
Finn RS, et al. Atezolizumab plus bevacizumab in unresectable hepatocellular carcinoma. <i>N Engl J Med.</i> 2020;382(20):1894-1905.	<a href="https://www.nejm.org/doi/10.1056/NEJMoa1915745">https://www.nejm.org/doi/10.1056/NEJMoa1915745</a>
Finn RS, et al. IMbrave150: Updated overall survival (OS) data from a global, randomized, open-label Phase III study of atezolizumab (atezo) + bevacizumab (bev) vs sorafenib (sor) in patients (pts) with unresectable hepatocellular carcinoma (HCC). <i>J Clin Oncol.</i> 2021;39(3_suppl):267.	<a href="https://ascopubs.org/doi/abs/10.1200/JCO.2021.39.3_suppl.267">https://ascopubs.org/doi/abs/10.1200/JCO.2021.39.3_suppl.267</a>
Golfieri R, et al. Patients with Barcelona Clinic liver cancer stages B and C hepatocellular carcinoma: Time for a subclassification. <i>Liver Cancer.</i> 2019;8(2):78-91.	<a href="https://pubmed.ncbi.nlm.nih.gov/31019899/">https://pubmed.ncbi.nlm.nih.gov/31019899/</a>
Jennings JJ, et al. Hepatotoxicity induced by immune checkpoint inhibitors: A comprehensive review including current and alternative management strategies <i>Expert Opin Drug Metab Toxicol.</i> 2019;15(3):231-244.	<a href="https://www.tandfonline.com/doi/full/10.1080/17425255.2019.1574744">https://www.tandfonline.com/doi/full/10.1080/17425255.2019.1574744</a>
Kelley RK, et al. Phase 3 (COSMIC-312) study of cabozantinib (C) in combination with atezolizumab (A) versus sorafenib (S) in patients (pts) with advanced hepatocellular carcinoma (aHCC) who have not received previous systemic anticancer therapy. <i>J Clin Oncol.</i> 2019;37(15_suppl):TPS4157-TPS4157.	<a href="https://ascopubs.org/doi/abs/10.1200/JCO.2019.37.15_suppl.TPS4157">https://ascopubs.org/doi/abs/10.1200/JCO.2019.37.15_suppl.TPS4157</a>

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Kudo M, et al. Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: a randomised phase 3 non-inferiority trial. <i>Lancet</i> . 2018;391(10126):1163-1173.	<a href="https://pubmed.ncbi.nlm.nih.gov/29433850/">https://pubmed.ncbi.nlm.nih.gov/29433850/</a>
Lenvatinib (Lenvima®) PI 2019.	<a href="http://www.lenvima.com/pdfs/prescribing-information.pdf">www.lenvima.com/pdfs/prescribing-information.pdf</a>
Li D, et al. Current treatment landscape for advanced hepatocellular carcinoma: Patient outcomes and the impact on quality of life. <i>Cancers (Basel)</i> . 2019;11(6):841.	<a href="https://pubmed.ncbi.nlm.nih.gov/31216701/">https://pubmed.ncbi.nlm.nih.gov/31216701/</a>
Llovet JM, et al. Lenvatinib (len) plus pembrolizumab (pembro) for the first-line treatment of patients (pts) with advanced hepatocellular carcinoma (HCC): Phase 3 LEAP-002 study. <i>J Clin Oncol</i> . 2019;37(15_suppl):TPS4152-TPS4152.	<a href="https://ascopubs.org/doi/abs/10.1200/jco.2019.37.15_suppl.tps4152">https://ascopubs.org/doi/abs/10.1200/jco.2019.37.15_suppl.tps4152</a>
Llovet JM, et al. Molecular therapies and precision medicine for hepatocellular carcinoma. <i>Nat Rev Clin Oncol</i> . 2018;15(10):599-616.	<a href="https://www.nature.com/articles/s41571-018-0073-4?WT.feed_name=subjects_cancer-therapy">https://www.nature.com/articles/s41571-018-0073-4?WT.feed_name=subjects_cancer-therapy</a>
Llovet JM, et al. Sorafenib in advanced hepatocellular carcinoma. <i>N Engl J Med</i> . 2008;359(4):378-390.	<a href="https://pubmed.ncbi.nlm.nih.gov/18650514/">https://pubmed.ncbi.nlm.nih.gov/18650514/</a>
Marrero JA, et al. Diagnosis, staging, and management of hepatocellular carcinoma: 2018 practice guidance by the American Association for the Study of Liver Diseases. <i>Hepatology</i> . 2018;68(2):723-750.	<a href="https://pubmed.ncbi.nlm.nih.gov/29624699/">https://pubmed.ncbi.nlm.nih.gov/29624699/</a>
Michot JM, et al. Immune-related adverse events with immune checkpoint blockade: A comprehensive review. <i>Eur J Cancer</i> . 2016;54:139-148.	<a href="https://www.ejancer.com/article/S0959-8049(15)01112-0/fulltext">https://www.ejancer.com/article/S0959-8049(15)01112-0/fulltext</a>
Miller ED, et al. Clinical characteristics and adverse impact of hepatotoxicity due to immune checkpoint inhibitors. <i>Am J Gastroenterol</i> . 2020;115(2):251-261.	<a href="https://pubmed.ncbi.nlm.nih.gov/31789632/">https://pubmed.ncbi.nlm.nih.gov/31789632/</a>
National Comprehensive Cancer Network (NCCN). Hepatobiliary cancers. Version 4.2021. 8.26.2021.	<a href="http://www.nccn.org/professionals/physician_gls/PDF/hepatobiliary.pdf">www.nccn.org/professionals/physician_gls/PDF/hepatobiliary.pdf</a>
Pugh RN, et al. Transection of the oesophagus for bleeding oesophageal varices. <i>Br J Surg</i> . 1973;60(8):646-649.	<a href="https://pubmed.ncbi.nlm.nih.gov/4541913/">https://pubmed.ncbi.nlm.nih.gov/4541913/</a>
Sangro B, et al. Nivolumab in sorafenib-naïve and -experienced patients with advanced hepatocellular carcinoma (HCC): Survival, hepatic safety, and biomarker assessments in CheckMate 040. Presented at AASLD The Liver Meeting 2017. Abstract 141.	<a href="https://www.natap.org/2017/AASLD/AASLD_34.htm">https://www.natap.org/2017/AASLD/AASLD_34.htm</a>
Siegel RL, et al. Cancer statistics, 2019. <i>CA Cancer J Clin</i> . 2019;69(1):7-34.	<a href="https://pubmed.ncbi.nlm.nih.gov/30620402/">https://pubmed.ncbi.nlm.nih.gov/30620402/</a>

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Sorafenib (Nexavar®) PI 2018.	<a href="http://labeling.bayerhealthcare.com/html/products/pi/Nexavar_PI.pdf">http://labeling.bayerhealthcare.com/html/products/pi/Nexavar_PI.pdf</a>
Villanueva A. Hepatocellular carcinoma. <i>N Engl J Med.</i> 2019;380(15):1450-1462.	<a href="https://pubmed.ncbi.nlm.nih.gov/30970190/">https://pubmed.ncbi.nlm.nih.gov/30970190/</a>
Yau T, et al. Efficacy and safety of nivolumab plus ipilimumab in patients with advanced hepatocellular carcinoma previously treated with sorafenib: The CheckMate 040 randomized clinical trial [published correction appears in <i>JAMA Oncol.</i> 2021 Jan 1;7(1):140]. <i>JAMA Oncol.</i> 2020;6(11):e204564. doi:10.1001/jamaoncol.2020.4564	<a href="https://pubmed.ncbi.nlm.nih.gov/33001135/">https://pubmed.ncbi.nlm.nih.gov/33001135/</a>
Yau T, et al. Nivolumab (NIVO) + ipilimumab (IPI) + cabozantinib (CABO) combination therapy in patients (pts) with advanced hepatocellular carcinoma (aHCC): Results from CheckMate 040. <i>J Clin Oncol.</i> 2020;38(4_suppl):478-478.	<a href="https://ascopubs.org/doi/abs/10.1200/JCO.2020.38.4_suppl.478">https://ascopubs.org/doi/abs/10.1200/JCO.2020.38.4_suppl.478</a>
Zhu AX, et al. Ramucirumab after sorafenib in patients with advanced hepatocellular carcinoma and increased $\alpha$ -fetoprotein concentrations (REACH-2): a randomised, double-blind, placebo-controlled, phase 3 trial. <i>Lancet Oncol.</i> 2019;20(2):282-296.	<a href="https://pubmed.ncbi.nlm.nih.gov/30665869/">https://pubmed.ncbi.nlm.nih.gov/30665869/</a>