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NCCN Guidelines Panel: Hepatobiliary Cancer

On behalf of the Society of Interventional Oncology, we respectfully request the NCCN Guidelines Panel for Hepatobiliary Cancer review the enclosed recommendations:

Specific Change 1: We respectfully urge the National Comprehensive Cancer Network (NCCN) to consider including durvalumab plus bevacizumab or lenvatinib plus pembrolizumab in the treatment guidelines HCC-G 1 of 2 as combination therapy for the subset of patients with hepatocellular carcinoma (HCC) who are receiving transarterial chemoembolization (TACE) and are at increased risk of disease progression. These recommendations are supported by level 1 evidence from the phase III EMERALD-1 and LEAP-012 studies, which demonstrate significant improvements in progression-free survival for unresectable HCC with these combination therapies..

Rationale: While both studies highlight superior disease control when combining local and systemic therapy, there were higher rates of treatment-related adverse events in the combination arms. Therefore, we reserve the addition of systemic therapy to patients with excellent performance status that are historically at higher risk for early disease progression, such as those with intermediate to advanced BCLC B disease and diffuse or infiltrative phenotypes.. Length of systemic treatment after TACE would be determined by the clinically observed benefit. The SIO acknowledges the complexity of HCC management which requires individualized treatment strategies and multidisciplinary involvement, particularly in more challenging disease presentations.

Specific Change 2: We request that HCC-G 1 of 2 be updated to clarify the following statement: "A dose of >400 Gy to 25% of the liver or less in patients with CTP A liver function is recommended."^{15 16} For anatomically limited disease, radiation segmentectomy with Y-90 or ablative dose stereotactic body radiation therapy (SBRT) should be considered.¹⁷⁻¹⁹ be change to "A dose of >400 Gy to 25% of the liver or less in patients with CTP A liver function is recommended."^{15 16} For anatomically limited disease, radiation segmentectomy with Y-90 glass microspheres—administered within the specified number of days post-calibration—should be considered."

Rationale: SBRT is already addressed in the Principles of Radiation Therapy section. This change clarifies that the recommendation pertains specifically to glass microspheres, which have a defined calibration window for optimal dosing.

References:

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- Durvalumab with or without bevacizumab with transarterial chemoembolisation in hepatocellular carcinoma (EMERALD-1): a multiregional, randomised, double-blind, placebo-controlled, phase 3 study. Sangro, BrunoAbdalla, Kathia et al. *The Lancet*, Volume 405, Issue 10474, 216 – 232
- De la Garza-Ramos C, Montazeri SA, LeGout JD, Lewis AR, Frey GT, Paz-Fumagalli R, Hallemeier CL, Rutenberg MS, Ashman JB, Toskich BB. Radiation Segmentectomy or Ablative External Beam Radiation Therapy as Initial Treatment for Solitary Hepatocellular Carcinoma: A Multicenter Experience. *J Hepatocell Carcinoma*. 2025 Mar 13;12:553-559. doi: 10.2147/JHC.S507267. PMID: 40099229; PMCID: PMC11912899.
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Thank you for your consideration of these recommendations.

Sincerely,

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