APPENDIX 4.
DELPHI ROUND AGREEMENT ON THE RECOMMENDATIONS OF SYSTEMIC THERAPY

The Delphi Panel rated each recommendation on a 9-point Likert scale from 1 (strongly disagree) to 9 (strongly agree). The mean value of each recommendation was calculated and categorized as appropriate (≥7), uncertain (4.0 to <7), or inappropriate (<4). A coefficient of variance ≥0.5 indicated non-consensus and the need for revision. The Delphi Panel agreement on each of the final recommendations of systemic therapy is as below.

	Recommendations	Mean	Coefficient of variance
1st line systemic therapies	1. Atezolizumab plus bevacizumab or durvalumab plus tremelimumab is recommended for systemic treatment-naïve patients with locally advanced unresectable or metastatic HCC not amenable to curative or loco-regional therapy who have Child-Pugh class A and ECOG performance status 0–1 (A1). If these two combination therapies cannot be applied, sorafenib or lenvatinib is recommended (A1).	9.00	0.00
	2. Sorafenib is considered for patients with HCC who have Child-Pugh class B7 (B1) or B8–9 (B2) if other conditions listed in Recommendation 1 are met.	8.67	0.06
2nd line systemic therapies	1. Regorafenib is recommended for patients with progressive HCC after at least 3 weeks of sorafenib (≥400 mg/day) treatment and with Child-Pugh class A and good performance status (ECOG score 0–1) (A1).	8.67	0.08
	2. Cabozantinib is recommended for patients with progressive HCC after first-line sorafenib or second-line systemic treatment and with Child-Pugh class A and good performance status (ECOG score 0–1) (A1).	8.44	0.10
	3. Ramucirumab is recommended for patients with progressive HCC after sorafenib or intolerance to sorafenib and with Child-Pugh class A, good performance status (ECOG score 0–1), and serum AFP level ≥400 ng/mL (A1).	8.67	0.08
	4. Pembrolizumab is recommended for patients with progressive HCC after sorafenib or intolerance to sorafenib and with Child-Pugh class A and good performance status (ECOG score 0–1) (B1).	8.44	0.09
	5. Either nivolumab plus ipilimumab combination therapy (B1) or nivolumab monotherapy (C1) can be considered for patients with progressive HCC after sorafenib or intolerance to sorafenib and with Child-Pugh class A and good performance status (ECOG score 0–1).	7.67	0.07
	6. Sorafenib, regorafenib, cabozantinib, ramucirumab (if serum AFP level ≥400 ng/mL), atezolizumab/bevacizumab, durvalumab/tremelimumab, pembrolizumab, nivolumab/ipilimumab, or nivolumab treatment can be tried for patients with progressive HCC after lenvatinib (D1).	7.67	0.13
	7. Sorafenib, lenvatinib, regorafenib, cabozantinib, durvalumab/tremelimumab, or nivolumab/ipilimumab can be tried for patients with progressive HCC after combination therapy with atezolizumab plus bevacizumab (D1).	7.67	0.13
	8. Sorafenib, lenvatinib, regorafenib, cabozantinib, ramucirumab (if serum AFP level ≥400 ng/mL), or atezolizumab/bevacizumab can be tried for patients with progressive HCC after combination therapy with durvalumab plus tremelimumab (D1).	7.44	0.14
Hepatic arterial infusion chemotherapy	1. HAIC may be considered for advanced HCC patients with preserved liver function and portal vein invasion without extrahepatic spread for whom first-line or second line systemic therapies, such as atezolizumab-bevacizumab, durvalumab-tremelimumab, sorafenib, lenvatinib, regorafenib, cabozantinib, ramucirumab, nivolumab-ipilimumab, or pembrolizumab, has failed or cannot be used (C2).	6.89	0.18

HCC, hepatocellular carcinoma; ECOG, Eastern Cooperative Oncology Group; AFP, alpha-fetoprotein.