

Figure S1 Forest plot analysis of factors associated with PFS. SYS+αPD-(L)1, SYS plus αPD-(L)1 antibody; SYS, systemic chemotherapy; αPD-(L)1, anti-programmed death-(ligand) 1 immunotherapy; HAIC+αPD-(L)1, HAIC-FO plus αPD-(L)1 antibody; HAIC-FO, HAIC with infusional FOLFOX regimens; HAIC, hepatic arterial infusion chemotherapy; FOLFOX, fluorouracil, leucovorin, and oxaliplatin; HR, hazard ratio; CI, confidence interval; HBV, hepatitis B virus; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9.

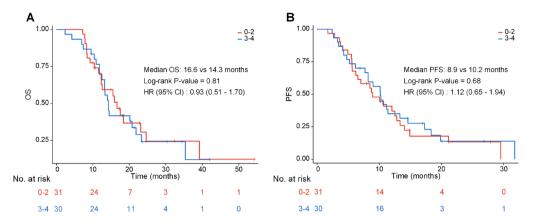


Figure S2 Kaplan-Meier survival analysis was conducted to assess the OS (A) and PFS (B) of uICC patients who experienced grade 0–2 and grade 3–4 AEs during HAIC plus αPD-(L)1 treatment as first-line treatments. OS, overall survival; HR, hazard ratio; CI, confidence interval; PFS, progression-free survival; uICC, unresectable intrahepatic cholangiocarcinoma; AEs, adverse events; HAIC, hepatic arterial infusion chemotherapy; αPD-(L)1, anti-programmed death-(ligand) 1 immunotherapy.

Table S1 The type of chemotherapy drug received by the SYS+αPD-(L)1 group of patients

| Variables                  | Before PSM (n=35) | After PSM (n=26) |
|----------------------------|-------------------|------------------|
| Gemcitabine                | 1 (2.9)           | 0 (0.0)          |
| Gemcitabine + cisplatin    | 23 (65.7)         | 19 (73.1)        |
| Gemcitabine + capecitabine | 3 (8.6)           | 2 (7.7)          |
| Gemcitabine + oxaliplatin  | 1 (2.9)           | 0 (0.0)          |
| Oxaliplatin + 5-FU         | 7 (20.0)          | 5 (19.2)         |
|                            |                   |                  |

Data are presented as n (%). SYS+ $\alpha$ PD-(L)1, SYS plus  $\alpha$ PD-(L)1 antibody; SYS, systemic chemotherapy;  $\alpha$ PD-(L)1, anti-programmed death-(ligand) 1 immunotherapy; PSM, propensity score matching; 5-FU, 5-fluorouracil.

Table S2 The baseline metastatic status of the two groups of patients before and after PSM

| Characteristics HAIC- | Before                | Before PSM          |                      | After PSM           |  |  |
|-----------------------|-----------------------|---------------------|----------------------|---------------------|--|--|
|                       | HAIC+αPD-(L)1 (n=147) | SYS+αPD-(L)1 (n=35) | HAIC+αPD-(L)1 (n=61) | SYS+αPD-(L)1 (n=26) |  |  |
| Lung                  | 17 (11.6)             | 7 (20.0)            | 11 (18.0)            | 5 (19.2)            |  |  |
| Peritoneum            | 8 (5.4)               | 9 (25.7)            | 4 (6.6)              | 3 (11.5)            |  |  |
| Bone                  | 11 (7.5)              | 8 (22.9)            | 8 (13.1)             | 4 (15.4)            |  |  |
| Adrenal gland         | 5 (3.4)               | 3 (8.6)             | 4 (6.6)              | 2 (7.7)             |  |  |
| diaphragm             | 1 (0.7)               | 0 (0.0)             | 0 (0.0)              | 0 (0.0)             |  |  |
| Pancreas              | 1 (0.7)               | 1 (2.9)             | 1 (1.6)              | 1 (3.8)             |  |  |

Data are presented as n (%). PSM, propensity score matching; HAIC+ $\alpha$ PD-(L)1, HAIC-FO plus  $\alpha$ PD-(L)1 antibody; HAIC-FO, HAIC with infusional FOLFOX regimens; HAIC, hepatic arterial infusion chemotherapy; FOLFOX, fluorouracil, leucovorin, and oxaliplatin;  $\alpha$ PD-(L)1, anti-programmed death-(ligand) 1 immunotherapy; SYS+ $\alpha$ PD-(L)1, SYS plus  $\alpha$ PD-(L)1 antibody; SYS, systemic chemotherapy.

Table S3 The 1- and 2-year OS rates for the two groups before and after PSM

| <u> </u>                   | Before PSM            |                     | After PSM            |                     |  |
|----------------------------|-----------------------|---------------------|----------------------|---------------------|--|
| Characteristics            | HAIC+αPD-(L)1 (n=147) | SYS+αPD-(L)1 (n=35) | HAIC+αPD-(L)1 (n=61) | SYS+αPD-(L)1 (n=26) |  |
| 1-year OS rate (95% CI), % | 70.3 (63.2–78.1)      | 51.7 (37.1–71.9)    | 69.8 (59.0–82.5)     | 40.0 (24.7–64.6)    |  |
| 2-year OS rate (95% CI), % | 33.8 (26.3–43.5)      | 13.7 (5.19–36.0)    | 27.3 (6.76–43.5)     | 17.1 (6.76–43.5)    |  |

OS, overall survival; PSM, propensity score matching; HAIC+ $\alpha$ PD-(L)1, HAIC-FO plus  $\alpha$ PD-(L)1 antibody; HAIC-FO, HAIC with infusional FOLFOX regimens; HAIC, hepatic arterial infusion chemotherapy; FOLFOX, fluorouracil, leucovorin, and oxaliplatin;  $\alpha$ PD-(L)1, antiprogrammed death-(ligand) 1 immunotherapy; SYS+ $\alpha$ PD-(L)1, SYS plus  $\alpha$ PD-(L)1 antibody; SYS, systemic chemotherapy; CI, confidence interval.

Table S4 The disease progression patterns of both groups before and after PSM

| Variables                            | Before PSM               |                        | After PSM |                         |                        |         |
|--------------------------------------|--------------------------|------------------------|-----------|-------------------------|------------------------|---------|
|                                      | HAIC+αPD-(L)1<br>(n=147) | SYS+αPD-(L)1<br>(n=35) | P value   | HAIC+αPD-(L)1<br>(n=61) | SYS+αPD-(L)1<br>(n=26) | P value |
| Progression of the primary tumor     | 9 (6.1)                  | 8 (22.9)               | 0.002*    | 3 (4.9)                 | 7 (26.9)               | 0.003*  |
| Newly developed intrahepatic lesions | 23 (15.6)                | 6 (17.1)               | 0.83      | 11(18.0)                | 5 (19.2)               | 0.90    |
| Progression of extrahepatic lesions  | 50 (34.0)                | 4 (11.4)               | 0.009*    | 18 (29.5)               | 3 (11.5)               | 0.07    |

<sup>\*,</sup> P<0.05. PSM, propensity score matching; HAIC+ $\alpha$ PD-(L)1, HAIC-FO plus  $\alpha$ PD-(L)1 antibody; HAIC-FO, HAIC with infusional FOLFOX regimens; HAIC, hepatic arterial infusion chemotherapy; FOLFOX, fluorouracil, leucovorin, and oxaliplatin;  $\alpha$ PD-(L)1, anti-programmed death-(ligand) 1 immunotherapy; SYS+ $\alpha$ PD-(L)1, SYS plus  $\alpha$ PD-(L)1 antibody; SYS, systemic chemotherapy.