**Supplementary Table 1.** Treatment details, detailed characteristics and outcome of patients (n = 47).

| ID  | PD-1 inhibitor (course) | Targeted agent | OS months | Response | Status |
|-----|-------------------------|----------------|-----------|----------|--------|
| 1   | Tislelizumab (14)       | Lenvatinib     | 20.3      | SD       | Death  |
| 2   | Tislelizumab (3)        | Anlotinib      | 4.5       | PD       | Death  |
| 3   | Sintilimab (9)          | Anlotinib      | 11.4      | PR       | Death  |
| 4   | Sintilimab (8)          | Lenvatinib     | 23.6      | PR       | Alive  |
| 5   | Tislelizumab (21)       | Lenvatinib     | 15.9      | CR       | Alive  |
| 6   | Tislelizumab (4)        | Anlotinib      | 7.4       | PR       | Death  |
| 7   | Tislelizumab (2)        | Sorafenib      | 3.1       | PD       | Death  |
| 8   | Tislelizumab (13)       | Lenvatinib     | 12.9      | SD       | Alive  |
| 9   | Tislelizumab (3)        | Lenvatinib     | 5.8       | SD       | Death  |
| 10  | Camrelizumab (3)        | Anlotinib      | 4.9       | SD       | Death  |
| 11  | Sintilimab (6)          | Anlotinib      | 20.1      | SD       | Death  |
| 12  | Sintilimab (6)          | Sorafenib      | 7.8       | PR       | Alive  |
| 13  | Tislelizumab (15)       | Lenvatinib     | 11.4      | PR       | Alive  |
| 14  | Tislelizumab (11)       | Anlotinib      | 13.3      | PR       | Alive  |
| 15  | Tislelizumab (10)       | Lenvatinib     | 13        | PR       | Alive  |
| 16  | Tislelizumab (4)        | Anlotinib      | 5.5       | SD       | Death  |
| 17  | Tislelizumab (7)        | Lenvatinib     | 12.7      | PR       | Alive  |
| 18  | Tislelizumab (9)        | Sorafenib      | 11.8      | PR       | Alive  |
| 19  | Sintilimab (8)          | Sorafenib      | 9.2       | SD       | Alive  |
| 20  | Tislelizumab (2)        | Lenvatinib     | 3.2       | PD       | Death  |
| 21  | Tislelizumab (3)        | Lenvatinib     | 3.7       | SD       | Death  |
| 22  | Sintilimab (5)          | Lenvatinib     | 8.3       | PR       | Alive  |
| 23  | Camrelizumab (6)        | Anlotinib      | 6.2       | SD       | Alive  |
| 24  | Tislelizumab (7)        | Lenvatinib     | 7.9       | PR       | Alive  |
| 25  | Tislelizumab (4)        | Lenvatinib     | 7.9       | SD       | Alive  |
| 26  | Sintilimab (5)          | Anlotinib      | 7.8       | SD       | Alive  |
| 27  | Tislelizumab (3)        | Anlotinib      | 4         | PR       | Death  |
| 28  | Camrelizumab (5)        | Anlotinib      | 10.8      | PR       | Death  |
| 29  | Tislelizumab (4)        | Lenvatinib     | 16.5      | SD       | Alive  |
| 30  | Sintilimab (3)          | Anlotinib      | 5.3       | SD       | Death  |
| 31  | Tislelizumab (22)       | Lenvatinib     | 24.7      | SD       | Alive  |
| 32  | Camrelizumab (3)        | Lenvatinib     | 13.7      | SD       | Alive  |
| 33  | Tislelizumab (9)        | Sorafenib      | 14        | SD       | Alive  |
| 34  | Tislelizumab (7)        | Sorafenib      | 10.9      | SD       | Death  |
| 35  | Tislelizumab (7)        | Anlotinib      | 7.2       | PR       | Alive  |
| 36  | Tislelizumab (8)        | Sorafenib      | 6.9       | PR       | Alive  |
| 37  | Camrelizumab (3)        | Lenvatinib     | 3.3       | SD       | Alive  |
| 38  | Camrelizumab (9)        | Regorafenib     | 6         | SD       | Alive  |
| 39  | Camrelizumab (2)        | Apatinib       | 3         | PD       | Alive  |
| 40  | Tislelizumab (7)        | Anlotinib      | 5.6       | SD       | Alive  |
| 41  | Tislelizumab (5)        | Lenvatinib     | 4.7       | SD       | Alive  |
|   | Treatment 1 | Treatment 2   | Duration | Status | Response |
|---|-------------|---------------|----------|--------|----------|
| 42| Camrelizumab (4) | Lenvatinib | 4.4      | SD     | Alive    |
| 43| Camrelizumab (5) | Anlotinib | 4.2      | SD     | Alive    |
| 44| Sintilimab (6) | Lenvatinib | 4.2      | SD     | Alive    |
| 45| Sintilimab (6) | Sorafenib | 4.2      | PR     | Alive    |
| 46| Camrelizumab (3) | Lenvatinib | 2.6      | SD     | Alive    |
| 47| Camrelizumab (2) | Regorafenib | 1.4      | SD     | Alive    |

Abbreviations: PD-1, programmed death 1; OS, overall survival; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease.
**Supplementary Table 2.** Univariate Cox regression analysis of progression-free survival and overall survival

| Variable                                | Progression-free survival | Overall survival |
|-----------------------------------------|----------------------------|-----------------|
|                                        | HR  | 95%CI | P   | HR  | 95%CI | P   |
| Sex (female/male)                       | 0.043 | 0.001-27.007 | 0.338 | 0.045 | 0.001-1177.192 | 0.551 |
| Age (≥60/<60 years)                     | 0.458 | 0.181-1.160 | 0.100 | 0.319 | 0.072-1.418 | 0.133 |
| Child-Pugh class (B/A)                  | 3.018 | 1.369-6.657 | 0.006 | 5.135 | 1.717-15.362 | 0.003 |
| Number of tumor (≥2/<2)                 | 5.180 | 1.648-16.277 | 0.005 | 5.780 | 1.251-26.708 | 0.025 |
| Tumor size (≥5/<5 cm)                   | 1.115 | 0.383-3.242 | 0.842 | 0.774 | 0.213-2.817 | 0.698 |
| AFP (≥400/<400 ng/ml)                   | 5.109 | 2.087-12.51 | < 0.001 | 3.789 | 1.283-11.188 | 0.016 |
| ECOG PS (1-2/0)                         | 1.386 | 0.628-3.060 | 0.419 | 1.542 | 0.518-4.595 | 0.437 |
| PD-L1+ CTC counts (≤2>2)                | 0.513 | 0.234-1.126 | 0.096 | 0.142 | 0.039-0.520 | 0.003 |
| BCLC stage (B/C)                        | 0.046 | 0.001-5792.205 | 0.608 | 0.046 | 0.001-8470444.981 | 0.752 |
| Portal vein invasion (no/yes)           | 0.639 | 0.084-4.846 | 0.665 | 0.044 | 0.001-6856.645 | 0.609 |
| HBV (positive/negative)                 | 1.275 | 0.508-3.200 | 0.605 | 1.016 | 0.275-3.755 | 0.981 |
| HCV (positive/negative)                 | 1.143 | 0.268-4.878 | 0.857 | 1.041 | 0.134-8.119 | 0.969 |
| Alcoholism (positive/negative)          | 1.755 | 0.793-3.883 | 0.165 | 1.510 | 0.533-4.277 | 0.438 |
| Lymph node metastasis (yes/no)          | 1.817 | 0.833-3.966 | 0.134 | 2.318 | 0.788-6.820 | 0.127 |
| Extrahepatic metastases (yes/no)        | 1.482 | 0.618-3.553 | 0.378 | 0.678 | 0.180-2.550 | 0.565 |
| Previous therapy (yes/no)               | 0.713 | 0.326-1.560 | 0.397 | 0.487 | 0.158-1.503 | 0.210 |

Abbreviations: HR, hazard ratio; CI, confidence interval; AFP, alpha fetoprotein; ECOG PS, Eastern Cooperative Oncology Group performance status; PD-L1, programmed death-ligand 1; CTCs, circulating tumor cells; BCLC, Barcelona Clinic Liver Cancer; HBV, hepatitis B virus; HCV, hepatitis C virus;
## Supplemental Table 3. Details of CTCs and PD-L1+ CTCs counts in the all patients

| ID | CTC counts | PD-L1+ CTC counts | CTC counts | PD-L1+ CTC counts | CTC counts | PD-L1+ CTC counts | ORR |
|----|-------------|-------------------|------------|-------------------|------------|-------------------|-----|
| 1  | 4           | 1                 | 2          | 1                 | -          | -                 | No  |
| 2  | 6           | 3                 | 0          | 0                 | -          | -                 | No  |
| 3  | 3           | 1                 | 0          | 0                 | -          | -                 | Yes |
| 4  | 0           | 0                 | -          | -                 | -          | -                 | Yes |
| 5  | 6           | 1                 | 0          | 0                 | -          | -                 | Yes |
| 6  | 8           | 5                 | 5          | 3                 | 3          | 1                 | Yes |
| 7  | 9           | 4                 | 3          | 2                 | -          | -                 | No  |
| 8  | 9           | 2                 | 3          | 1                 | 3          | 1                 | No  |
| 9  | 6           | 2                 | 3          | 1                 | -          | -                 | No  |
| 10 | 7           | 2                 | 6          | 3                 | -          | -                 | No  |
| 11 | 3           | 2                 | 1          | 1                 | -          | -                 | No  |
| 12 | 5           | 1                 | 2          | 1                 | -          | -                 | Yes |
| 13 | 4           | 1                 | 1          | 0                 | 3          | 1                 | Yes |
| 14 | 7           | 1                 | 6          | 3                 | 5          | 2                 | Yes |
| 15 | 2           | 0                 | 1          | 0                 | 3          | 1                 | Yes |
| 16 | 5           | 1                 | 1          | 1                 | -          | -                 | No  |
| 17 | 6           | 1                 | 4          | 1                 | -          | -                 | Yes |
| 18 | 6           | 1                 | 2          | 0                 | -          | -                 | Yes |
| 19 | 8           | 1                 | 3          | 2                 | -          | -                 | No  |
| 20 | 7           | 2                 | 9          | 4                 | -          | -                 | No  |
| 21 | 8           | 2                 | 2          | 1                 | -          | -                 | No  |
| 22 | 9           | 1                 | 5          | 0                 | -          | -                 | Yes |
| 23 | 5           | 2                 | 0          | 0                 | 2          | 1                 | No  |
| 24 | 3           | 1                 | 0          | 0                 | 2          | 1                 | Yes |
| 25 | 3           | 1                 | 0          | 0                 | -          | -                 | No  |
| 26 | 8           | 5                 | -          | -                 | -          | -                 | No  |
| 27 | 9           | 2                 | 5          | 1                 | 0          | 0                 | Yes |
| 28 | 7           | 2                 | 2          | 1                 | -          | -                 | Yes |
| 29 | 4           | 1                 | 1          | 0                 | -          | -                 | No  |
| 30 | 5           | 1                 | 3          | 2                 | -          | -                 | No  |
| 31 | 0           | 0                 | 0          | 0                 | -          | -                 | No  |
| 32 | 4           | 1                 | -          | -                 | -          | -                 | No  |
| 33 | 3           | 2                 | 4          | 2                 | -          | -                 | No  |
| 34 | 6           | 2                 | -          | -                 | -          | -                 | No  |
| 35 | 6           | 1                 | 0          | 0                 | 0          | 0                 | Yes |
| 36 | 5           | 2                 | 4          | 1                 | 3          | 1                 | Yes |
| 37 | 7           | 2                 | 2          | 1                 | -          | -                 | No  |
| 38 | 6           | 2                 | 2          | 1                 | 2          | 1                 | No  |
| 39 | 6           | 1                 | 2          | 2                 | -          | -                 | No  |
|   | 5  | 1  | 2  | 1  | 1  | 1  | No |
|---|----|----|----|----|----|----|----|
| 41| 6  | 2  | 2  | 1  | -  | -  | No |
| 42| 9  | 2  | 4  | 3  | -  | -  | No |
| 43| 9  | 2  | 3  | 1  | 2  | 1  | No |
| 44| 4  | 2  | -  | -  | -  | -  | No |
| 45| 5  | 1  | 2  | 1  | 3  | 2  | Yes|
| 46| 8  | 2  | 3  | 2  | -  | -  | No |
| 47| 6  | 4  | 3  | 1  | -  | -  | No |

Abbreviations: CTC, circulating tumor cells; PD-L1, programmed death-ligand 1; ORR, objective response rate.
Supplementary Fig. 1. Kaplan-Meier plots: (A) progression-free survival and (B) overall survival based on PD-L1 expression on CTCs at T1. Abbreviations: HR, hazard ratio; CI, confidence interval; CTCs, circulating tumor cells; PD-L1, programmed death-ligand 1.