**Supplementary Table 1.** Comparing baseline characteristics of advanced hepatocellular carcinoma patients received ramucirumab in 2nd line and 3rd or later line

|  |  |  |  |
| --- | --- | --- | --- |
|  | **2nd line**  **(n = 13)** | **3rd or later line**  **(n = 24)** | **P-value** |
| **Sex,** Male | 10 (76.9%) | 21 (87.5%) | 0.643 |
| **Age,** ≥73 | 8 (61.5%) | 11 (45.8%) | 0.495 |
| **Child-Pugh class,** B | 6 (46.2%) | 14 (58.3%) | 0.475 |
| **AFP,** ≥1900 | 5 (8.5%) | 14 (58.5%) | 0.475 |
| **BCLC,** C | 9 (69.2%) | 12 (50.0%) | 0.315 |
| **Tumor size, >**50mm | 8 (61.5%) | 13 (54.2%) | 0.739 |
| **Tumor number,** >7 | 7 (53.8%) | 14 (58.5%) | 1.000 |
| **MVI** | 6 (46.2%) | 2 (8.3%) | 0.013 |
| **EHM** | 6 (46.2%) | 12 (50.0%) | 1.000 |

AE, adverse event; BCLC, Barcelona clinic liver cancer; MVI, macrovascular invasion; EHM, extrahepatic metastasis

**Supplementary Table 2.** Best response, objective response rate, and disease control rate during ramucirumab treatment.

|  |  |
| --- | --- |
|  | **All patients (n= 37)** |
| **RECIST**  Complete response  Partial response  Stable disease  Progressive disease  Objective response rate  Disease control rate | 0  1 (2.7%)  18 (48.6%)  14 (37.8%)  1 (2.7%)  19 (51.4%) |
| **mRECIST**  Complete response  Partial response  Stable disease  Progressive disease  Objective response rate  Disease control rate | 0  7 (19.0%)  11 (29.7%)  13 (35.1%)  7 (19.0%)  17 (45.9%) |

RECIST, Response Evaluation Criteria in Solid Tumors; mRECIST, modified RECIST

**Supplementary Table 3.** Comparing overall survival and progression free survival by clinical parameters inadvanced hepatocellular carcinoma patients received ramucirumab

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **OS** | | | **PFS (RECIST)** | | | **PFS (mRECIST)** | | |
|  | **Median (month)** | **95%CI** | **p-value** | **Median (month)** | **95%CI** | **p-value** | **Median (month)** | **95%CI** | **p-value** |
| **Tumor number >7**  Absent  Present | 14.1  6.2 | 7.43-NA  3.68-12.49 | 0.175 | 2.7  3.7 | 4.54-7.29  1.45-NA | 0.860 | 3.2  3.6 | 1.54-7.30  1.44-NA | 0.998 |
| **AFP >1900 ng/mL**  Absent  Present | 10.4  10.3 | 4.63-NA  1.97-NA | 0.874 | 3.6  2.7 | 1.45-8.18  1.84-NA | 0.860 | 3.5  3.4 | 1.45-10.35  1.84-6.37 | 0.617 |
| **Child-Pugh B**  Absent  Present | 12.5  1.64 | 7.43-19.41  0.69-NA | <0.001 | 2.7  3.5 | 1.61-7.30  0.69-NA | 0.803 | 3.2  3.5 | 1.61-6.37  0.69-NA | 0.955 |
| **BCLC C**  Absent  Present | 12.5  10.3 | 1.97-NA  4.40-19.42 | 0.742 | 6.9  2.6 | 1.84-NA  1.02-8.28 | 0.785 | 5.2  2.3 | 1.84-NA  1.02-3.50 | 0.659 |
| **MVI**  Absent  Present | 12.5  8.2 | 5.16-14.62  0.79-NA | 0.601 | 2.7  3.6 | 1.84-7.29  0.89-NA | 0.370 | 3.2  3.6 | 1.84-6.37  0.89-NA | 0.395 |
| **EHM**  Absent  Present | 9.0  12.6 | 3.75-14.09  3.68-19.42 | 0.360 | 6.9  1.8 | 1.84-NA  0.99-8.28 | 0.216 | 5.2  1.8 | 2.30-7.29  0.99-3.45 | 0.157 |

BCLC, Barcelona clinic liver cancer; MVI, macrovascular invasion; EHM, extrahepatic metastasis; OS, overall survival; PFS, progression free survival; RECIST, Response Evaluation Criteria in Solid Tumors; mRECIST, modified RECIST

**Supplementary Table 4.** Multivariate analysis of OS, PFS during ramucirumab treatment; COX proportional hazards analysis

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **OS** | | | **PFS (RECIST)** | | | **PFS (mRECIST)** | | |
| **Variables** | **Hazard ratio** | **95%CI** | **p-value** | **Hazard ratio** | **95%CI** | **p-value** | **Hazard ratio** | **95%CI** | **p-value** |
| **Treatment line**  2nd line  3rd or later line | Reference  1.63 | 0.284-2.226 | 0.370 | Reference  0.51 | 0.149-1.722 | 0.276 | Reference  0.43 | 0.127-1.486 | 0.184 |
| **Child-Pugh class**  A  B | Reference  4.76 | 1.61-14.110 | <0.01 | Reference  1.24 | 0.265-5.800 | 0.786 | Reference  1.10 | 0.235-5.145 | 0.904 |
| **MVI**  Absent  Present | Reference  0.80 | 0.561-4.735 | 0.663 | Reference  0.66 | 0.236-1.882 | 0.443 | Reference  0.48 | 0.173-1.354 | 0.167 |

OS, overall survival; PFS, progression free survival; RECIST, Response Evaluation Criteria in Solid Tumors; mRECIST, modified RECIST; MVI, macrovascular invasion