**Supplementary table 1. Comparisons of the patient selection criteria for relevant published RCTs.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Author (year)** | **Study design** | **Sample size TACE/TACE-S** | **Patient selection** | | |
| **Tumor burden** | **Liver function** | **Performance status** |
| Kudo M, et al. (2011) [1] | PhaseⅢ | 229/229 | Tumor size ≤7cm Tumor number ≤10 | Child-Pugh A | ECOG 0-1 score |
| Lencioni R, et al. (2016) [2] | PhaseⅡ | 153/154 | Unresectable multinodular | Child-Pugh A (without ascites) | ECOG 0 score |
| Meyer T, et al (2017) [3] | PhaseⅢ | 156/157 | Not a candidate for resection or transplantation | Child-Pugh A | ECOG 0-1 score |
| Kudo M, et al. (2018) [4] | PhaseⅡ | 76/80 | Tumor size ≤10cm Tumor number ≤10 | Child-Pugh A/B7 | ECOG 0-1 score |
| Abbreviations: RCTs, randomized controlled trials; TACE, transarterial chemoembolization; TACE-S, the combination therapy of TACE and sorafenib; ECOG, Eastern Cooperative Oncology Group. | | | | | |

**Supplementary table 2. Baseline characteristics for the study patients with available TTP.**

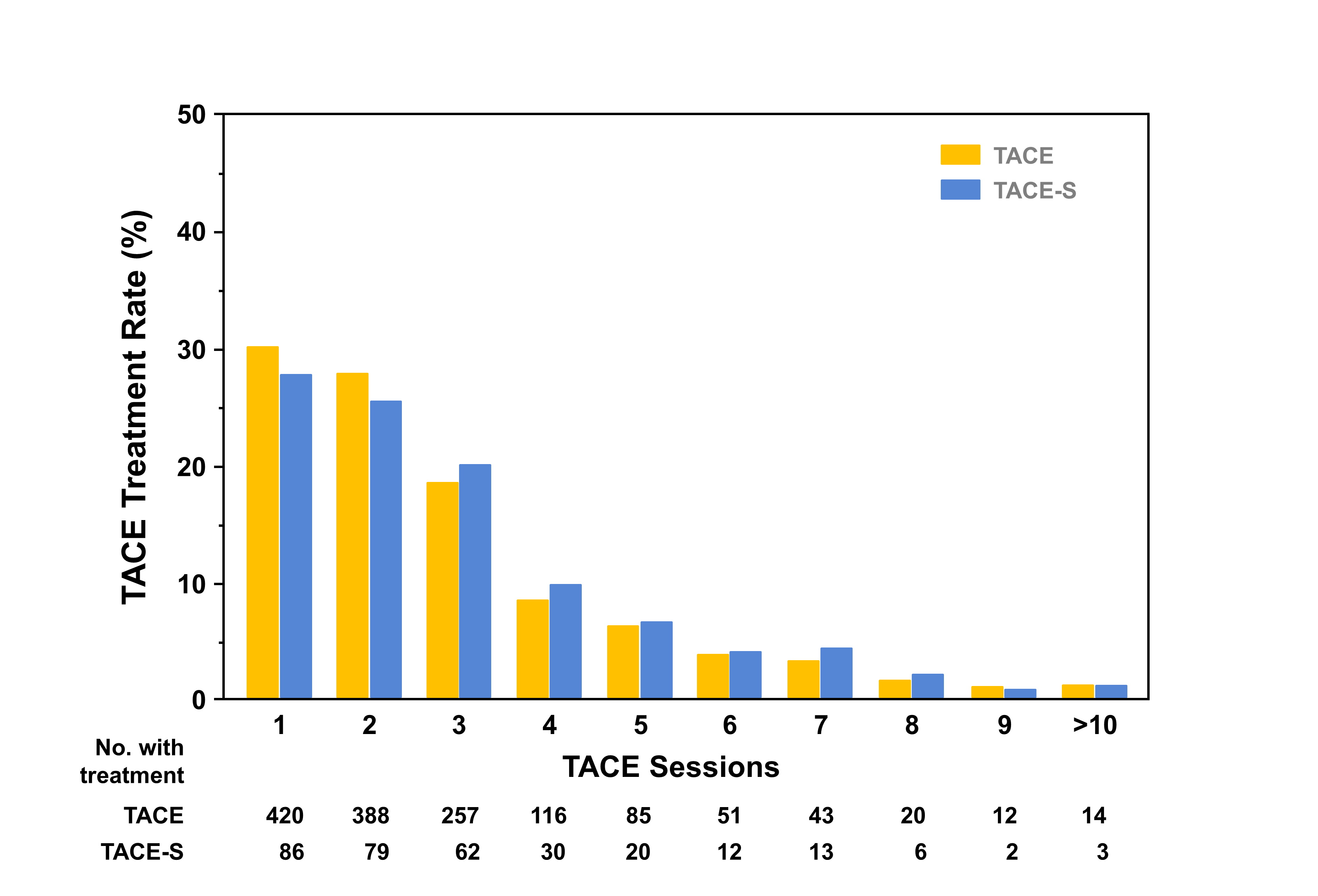
|  |  |  |  |
| --- | --- | --- | --- |
| **Baseline characteristics** | **Total** | **TACE** | **TACE-S** |
| Patients, n | 516 | 307 | 209 |
| Age, mean ± sd | 54.0 ± 12.1 | 54.5 ± 12.0 | 53.2 ± 12.2 |
| Gender, n (%) |  |  |  |
| Male | 426 (82.6) | 252 (82.1) | 174 (83.3) |
| Female | 90 (17.4) | 55 (17.9) | 35 (16.7) |
| Etiology, n (%) |  |  |  |
| HBV | 434 (84.1) | 262 (85.3) | 172 (82.3) |
| HCV | 23 (4.5) | 12 (3.9) | 11 (5.3) |
| Others | 59 (11.4) | 33 (10.7) | 26 (12.4) |
| Antiviral treatment, n (%) | 422 (81.3) | 249 (81.1) | 173 (82.8) |
| BCLC stage, n (%) |  |  |  |
| A | 61 (11.8) | 34 (11.1) | 27 (12.9) |
| B | 285 (55.2) | 185 (60.2) | 100 (47.8) |
| C | 170 (32.9) | 88 (28.7) | 82 (39.2) |
| Performance status, ECOG score, n (%)\* |  |  |  |
| 0 | 346 (67.1) | 219 (71.3) | 127 (60.8) |
| 1 | 170 (32.9) | 88 (28.7) | 82 (39.2) |
| Child-Pugh score, n (%) |  |  |  |
| 5 | 391 (75.8) | 229 (74.6) | 162 (77.5) |
| 6 | 99 (19.2) | 62 (20.2) | 37 (17.7) |
| 7 | 26 (5.0) | 16 (5.2) | 10 (4.8) |
| Ascites, n (%) |  |  |  |
| Negative | 476 (92.2) | 283 (92.2) | 193 (92.3) |
| Positive | 40 (7.8) | 24 (7.8) | 16 (7.7) |
| AFP, ng/mL, n (%) |  |  |  |
| ≤200 | 273 (52.9) | 167 (54.4) | 106 (50.7) |
| >200 | 243 (47.1) | 140 (45.6) | 103 (49.3) |
| Tumor number, median [IQR]\* | 1 [1-2] | 1[1-2] | 1 [1-2] |
| Tumor size, cm, mean ± sd\* | 7.8 ± 3.9 | 7.5 ± 3.7 | 8.3 ± 3.7 |
| International normalized ratio, mean ± sd | 1.12 ± 0.15 | 1.13 ± 0.16 | 1.10 ± 0.13 |
| Alanine aminotransferase, U/L, mean ± sd | 44.9 ± 34.0 | 43.7 ± 29.8 | 46.7 ± 39.4 |
| Aspartate aminotransferase, U/L, mean ± sd | 53.2 ± 37.3 | 52.0 ± 36.9 | 55.0 ± 37.8 |
| Albumin, g/L, mean ± sd | 39.4 ± 5.1 | 39.1 ± 5.1 | 39.7 ± 5.1 |
| Total bilirubin, μmol/L, mean ± sd | 16.8 ± 7.5 | 16.9 ± 7.9 | 16.5 ± 6.9 |
| Urea nitrogen, mmol/L, mean ± sd\* | 5.2 ± 1.5 | 5.4 ± 1.5 | 5.0 ± 1.4 |
| Serum creatinine, umol/L, mean ± sd | 85.5 ± 19.6 | 85.3 ± 19.2 | 85.8 ± 20.2 |
| Abbreviations: TTP, time to progression; TACE, transarterial chemoembolization; TACE-S, combining transarterial chemoembolization and sorafenib; sd, standard deviation; HBV, hepatitis B virus; HCV, hepatitis C virus; BCLC, Barcelona Clinic Liver Cancer; ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range; AFP, alpha-fetoprotein; TACE, transarterial chemoembolization; TACE-S, the combination therapy of TACE and sorafenib.  \*Variables with significantly difference between patients treated with TACE and TACE-S (P<0.05). | | | |
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**Supplementary table 3. Baseline characteristics for the candidates and non-candidates.**

|  |  |  |
| --- | --- | --- |
| **Study cohort** | **OS Analyses** | **TTP Analyses** |
|
| **Candidates** | | |
| Patients, n | 1051 | 330 |
| Age, years, mean ± sd | 55.9 ± 12.3 | 53.8 ± 12.1 |
| Gender, male/female, n (%) | 889 (84.6)/162 (15.4) | 278 (84.2)/52 (15.8) |
| Etiology, HBV/HCV/others, n (%) | 860 (81.8)/34 (3.2)/157 (14.9) | 272 (82.4)/12 (3.6)/46 (13.9) |
| Performance status, ECOG score 0/1, n (%) | 744 (70.8)/307 (29.2) | 235 (71.2)/95 (28.8) |
| Child-Pugh, A5/A6/B7, n (%) | 863 (82.1)/138 (13.1)/50 (4.8) | 273 (82.7)/42 (12.7)/15 (4.5) |
| Ascites, negative/positive, n (%) | 1008 (95.9)/43 (4.1) | 302 (91.5)/28 (8.5) |
| AFP, ≤200/>200 ng/mL, n (%) | 563 (53.6)/488 (46.4) | 171 (51.8)/159 (48.2) |
| Tumor number, median [IQR] | 2.1 ± 1.9/1 [1-2] | 1.9 ± 1.2/1 [1-2] |
| Tumor size, cm, mean ± sd | 7.6 ± 3.1 | 7.7 ± 2.7 |
| International normalized ratio, mean ± sd | 1.15 ± 0.11 | 1.09 ± 0.13 |
| Alanine aminotransferase, U/L, mean ± sd | 47.9 ± 37.2 | 43.8 ± 28.8 |
| Aspartate aminotransferase, U/L, mean ± sd | 53.3 ± 36.2 | 49.8 ± 36.7 |
| Albumin, g/L, mean ± sd | 40.6 ± 5.2 | 40.9 ± 5.1 |
| Total bilirubin, μmol/L, mean ± sd | 16.3 ± 7.6 | 15.7 ± 6.8 |
| Urea nitrogen, mmol/L, mean ± sd | 5.3 ± 1.6 | 5.3 ± 1.5 |
| Serum creatinine, umol/L, mean ± sd | 77.3 ± 19.3 | 88.0 ± 218.6 |
| Treatment, TACE alone/TACE-S, n (%) | 845 (80.4)/206 (19.6) | 192 (58.2)/138 (41.8) |
| **Non-candidates** | | |
| Patients, n | 668 | 186 |
| Age, years, mean ± sd | 56.5 ± 11.9 | 54.2 ± 12.1 |
| Gender, male/female, n (%) | 561 (84.0)/107 (16.0) | 148 (79.6)/38 (20.4) |
| Etiology, HBV/HCV/others, n (%) | 641 (82.3)/26 (3.3)/112 (14.4) | 162 (87.1)/11 (5.9)/13 (7.0) |
| Performance status, ECOG score 0/1, n (%) | 407 (60.9)/261 (39.1) | 111 (59.7)/75 (40.3) |
| Child-Pugh, A5/A6/B7, n (%) | 416 (62.3)/201 (30.1)/51 (7.6) | 118 (63.4)/57 (30.6)/11 (5.9) |
| Ascites, negative/positive, n (%) | 638 (95.5)/30 (4.5) | 174 (93.5)/12 (6.5) |
| AFP, ≤200/>200 ng/mL, n (%) | 379 (56.1)/289 (43.3) | 102 (54.8)/84 (45.2) |
| Tumor number, median [IQR] | 2.5 ± 2.5/1 [1-3] | 2.2 ± 2.3/1 [1-2] |
| Tumor size, cm, mean ± sd | 7.9 ± 5.1 | 8.1 ± 5.0 |
| International normalized ratio, mean ± sd | 1.12 ± 0.15 | 1.16 ± 0.16 |
| Alanine aminotransferase, U/L, mean ± sd | 51.8 ± 46.8 | 46.9 ± 41.7 |
| Aspartate aminotransferase, U/L, mean ± sd | 63.2 ± 47.7 | 59.3 ± 37.5 |
| Albumin, g/L, mean ± sd | 36.5 ± 3.9 | 36.6 ± 3.9 |
| Total bilirubin, μmol/L, mean ± sd | 19.1 ± 9.1 | 18.7 ± 8.3 |
| Urea nitrogen, mmol/L, mean ± sd | 5.3 ± 1.7 | 5.2 ± 1.5 |
| Serum creatinine, umol/L, mean ± sd | 75.0 ± 20.9 | 81.2 ± 20.6 |
| Treatment, TACE alone/TACE-S, n (%) | 561 (84.0)/107 (16.0) | 115 (61.8)/71 (38.2) |
| Abbreviations: OS, overall survival; TTP, time to progression; sd, standard deviation; HBV, hepatitis B virus; HCV, hepatitis C virus; BCLC, Barcelona Clinic Liver Cancer; ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range; AFP, alpha-fetoprotein; TACE, transarterial chemoembolization; TACE-S, the combination therapy of TACE and sorafenib.  Patients with either moderate tumor burden or low ALBI score were defined as candidates; otherwise, none-candidates. | | |

**Supplementary figure 1. Comparisons of TACE sessions between patients treated with TACE and TACE-S.**

TACE, transarterial chemoembolization; TACE-S, combining TACE and sorafenib.



**Supplementary figure 2. Outcome comparisons between TACE and TACE-S for subsets with different tumor burden in terms of OS unadjusted (A) and adjusted for propensity score (B), as well as TTP unadjusted (C) and adjusted for propensity score (D).**

TACE, transarterial chemoembolization; TACE-S, combining TACE and sorafenib; OS, overall survival; TTP, time to progression; HR, hazard ratio; CI, confidence intervals.

Low tumor burden, ≤7, moderate tumor burden, >7 and ≤12, high tumor burden, >12.



**Supplementary figure 3. Outcome comparisons between TACE and TACE-S for subsets with different ALBI score in terms of OS unadjusted (A) and adjusted for propensity score (B), as well as TTP unadjusted (C) and adjusted for propensity score (D).**

TACE, transarterial chemoembolization; TACE-S, combining TACE and sorafenib; ALBI, albumin-bilirubin; OS, overall survival; TTP, time to progression; HR, hazard ratio; CI, confidence intervals.

Low ALBI score, ≤-2.8, high ALBI score, >-2.8.



**Supplementary figure 4. Imaging assessments after 4-8 weeks of first TACE (532 available patients in TACE alone and 209 in TACE-S) varied with tumor burden.**

ALBI, albumin-bilirubin; TACE, transarterial chemoembolization; TACE-S, combining TACE and sorafenib.



**Supplementary figure 5. Comparisons of sorafenib duration in different ALBI score (122 and 191 TACE-S treated patients in low and high ALBI subsets).**

TACE, transarterial chemoembolization; TACE-S, combining TACE and sorafenib; objective response, complete or partial response; disease control, free of progression.



**Supplementary figure 6. Correlations between the final findings and the patient selection (ratio of the candidates) in previous studies, namely, Post-TACE (negative), SPACE (negative), TACE-2 (negative), TACTICS (positive), as well as our study (negative for the whole cohort).**

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