

**Table SI.** Results of full search strategy of database.

| Database       | Search strategy  |
|----------------|--|
| PubMed         | <p>#1 “Carcinoma, Hepatocellular”[Mesh] OR “Liver Neoplasms”[Mesh] OR HCC[Title/Abstract]<br/> #2 (((carcinoma*[Title/Abstract]) OR (cancer*[Title/Abstract])) OR (tumor*[Title/Abstract])) OR (malign*[Title/Abstract]) OR (neoplasm*[Title/Abstract])<br/> #3 ((liver*[Title/Abstract]) OR (hepatic*[Title/Abstract])) OR (hepato*[Title/Abstract])<br/> #4 #1 OR (#2 AND #3)<br/> #5 ((sorafenib[Title/Abstract]) OR (nexavar[Title/Abstract])) OR (tosylate[Title/Abstract])<br/> #6 ((lenvatinib[Title/Abstract]) OR (lenvima[Title/Abstract])) OR (E7080[Title/Abstract])<br/> #7 ((((((“Chemoembolization, Therapeutic”[Mesh]) OR (Chemoemboli*[Title/Abstract])) OR (emboli*[Title/Abstract])) OR (TACE[Title/Abstract])) OR (TAE[Title/Abstract])) OR (transarterial[Title/Abstract])) OR (transcatheter[Title/Abstract])<br/> #8 #5 OR #6 OR #7<br/> #9 (“Clinical Trials as Topic”[Mesh] OR “Clinical Trials as Topic”[Mesh] OR "Randomized Controlled Trials as Topic"[Mesh]) OR (((((random*[Title/Abstract]) OR (clinical trial*[Title/Abstract])) OR (placebo[Title/Abstract])) OR (controlled trial*[Title/Abstract])) OR (RCT[Title/Abstract]))<br/> #10 #4 AND #8 AND #9</p> |
| Cochrane       | <p>#1 MeSH descriptor: [Carcinoma, Hepatocellular] explode all trees<br/> #2 MeSH descriptor: [Liver Neoplasms] explode all trees<br/> #3 (carcinoma*):ti,ab,kw OR (cancer*):ti,ab,kw OR (tumor*):ti,ab,kw OR (malign*):ti,ab,kw AND (neoplasm*):ti,ab,kw<br/> #4 (liver*):ti,ab,kw OR (hepatic*):ti,ab,kw OR (hepato*):ti,ab,kw<br/> #5 #3 AND #4<br/> #6 #1 OR #2 OR #5<br/> #7 (sorafenib):ti,ab,kw OR (nexavar):ti,ab,kw OR (tosylate):ti,ab,kw<br/> #8 (lenvatinib):ti,ab,kw OR (lenvima):ti,ab,kw OR (E7080):ti,ab,kw<br/> #9 MeSH descriptor: [Chemoembolization, Therapeutic] explode all trees<br/> #10 (Chemoemboli*):ti,ab,kw OR (emboli*):ti,ab,kw OR (TACE):ti,ab,kw OR (transarterial):ti,ab,kw OR (transcatheter):ti,ab,kw<br/> #11 #7 OR #8 OR #9 OR #10<br/> #12 MeSH descriptor: [Randomized Controlled Trial] explode all trees<br/> #13 (random*):ti,ab,kw OR (clinical trial*):ti,ab,kw OR (placebo):ti,ab,kw OR (controlled trial*):ti,ab,kw OR (RCT):ti,ab,kw<br/> #14 #12 OR #13<br/> #15 #6 AND #11 AND #14</p>   |
| Embase         | <p>#1 ‘liver cancer’/exp OR ‘liver cancer’ OR ‘liver cell carcinoma’/exp OR ‘liver cell carcinoma’<br/> #2 carcinoma*:ab,kw,ti OR cancer*:ab,kw,ti OR tumor*:ab,kw,ti OR malign*:ab,kw,ti OR neoplasm*:ab,kw,ti<br/> #3 liver*:ab,kw,ti OR hepatic*:ab,kw,ti OR hepato*:ab,kw,ti<br/> #4 #1 OR (#2 AND #3)<br/> #5 ‘sorafenib’:ab,kw,ti OR ‘nexavar’:ab,kw,ti OR ‘tosylate’:ab,kw,ti<br/> #6 ‘lenvatinib’:ab,kw,ti OR ‘lenvima’:ab,kw,ti OR ‘e7080’:ab,kw,ti<br/> #7 ‘chemoembolization’/exp OR ‘chemoembolization’ OR ‘chemoemboli*’:ab,kw,ti OR ‘emboli*’:ab,kw,ti OR ‘tace’:ab,kw,ti OR ‘transarterial’:ab,kw,ti OR ‘transcatheter’:ab,kw,ti<br/> #8 #5 OR #6 OR #7<br/> #9 ‘randomized controlled trial’/exp OR ‘random*’:ab,kw,ti OR ‘clinical trial*’:ab,kw,ti OR ‘placebo’:ab,kw,ti OR ‘controlled trial*’:ab,kw,ti OR ‘rct’:ab,kw,ti<br/> #10 #4 AND #8 AND #9</p>   |
| Web of Science | <p>#1 (TS=(liver cancer)) OR TS=(hepatocellular carcinoma)<br/> #2 (((((TS=(carcinoma*)) OR TS=(cancer*)) OR TS=(tumor*)) OR TS=(malign*)) OR TS=(neoplasm*))<br/> #3 ((TS=(liver*)) OR TS=(hepatic*)) OR TS=(hepato*)<br/> #4 #1 OR (#2 AND #3)<br/> #5 (((((TS=(sorafenib)) OR TS=(nexavar)) OR TS=(tosylate)) OR TS=(lenvatinib)) OR TS=(lenvima)) OR TS=(E7080)<br/> #6 (((TS=(chemoembolization)) OR TS=(emboli*)) OR TS=(TACE)) OR TS=(transarterial)) OR</p>  |

|  |  |
|--|--|
|  | TS=(transcatheter)<br>#7 #5 OR #6<br>#8 (((((TS=(randomized controlled trial)) OR TS=(random*)) OR TS=(clinical trial*)) OR<br>TS=(placebo)) OR TS=(controlled trial*)) OR TS=(RCT)<br>#9 #4 AND #7 AND #8 |
|--|--|

**Table SII.** Top three most common grade 3/4 adverse events of treatments.

| A, Sorafenib + TACE     |             |
|-------------------------|-------------|
| AEs                     | Patients, % |
| Elevated AST            | 21.6        |
| Hypertension            | 15.4        |
| Abdominal pain          | 8.3         |
| B, TACE                 |             |
| AEs                     | Patients, % |
| Elevated AST            | 10.9        |
| Abdominal pain          | 9.4         |
| Elevated ALT            | 8.2         |
| C, Lenvatinib           |             |
| AEs                     | Patients, % |
| Hypertension            | 22.3        |
| Weight decrease         | 7.4         |
| Hyperbilirubinemia      | 5.6         |
| D, Sorafenib            |             |
| AEs                     | Patients, % |
| Hypertension            | 11.8        |
| Hand-foot skin reaction | 11.4        |
| Elevated AST            | 7.2         |

TACE, transarterial chemoembolization; AEs, adverse events; AST, aspartate transaminase; ALT, alanine aminotransferase.

**Table III.** Indirect comparisons of grade 3/4 adverse events among different treatments.

| A, Hand-foot skin reaction         |                     |                      |                   |                  |
|------------------------------------|---------------------|----------------------|-------------------|------------------|
| Drug treatment                     | Lenvatinib + TACE   | Sorafenib + TACE     | TACE              | Lenvatinib       |
| Sorafenib + TACE                   | 0.28 (0.07-1.03)    |                      |                   |                  |
| TACE                               | 18.35 (2.89-184.05) | 64.83 (19.28-457.15) |                   |                  |
| Lenvatinib                         | 1.06 (0.36-3.18)    | 3.81 (1.66-9.06)     | 0.06 (0.01-0.26)  |                  |
| Sorafenib                          | 0.26 (0.08-0.88)    | 0.95 (0.50-1.75)     | 0.01 (0-0.06)     | 0.25 (0.13-0.43) |
| B, Diarrhea                        |                     |                      |                   |                  |
| Drug treatment                     | Lenvatinib + TACE   | Sorafenib + TACE     | TACE              | Lenvatinib       |
| Sorafenib + TACE                   | 1.03 (0.22-4.80)    |                      |                   |                  |
| TACE                               | 5.80 (1.01-33.96)   | 5.53 (2.67-13.65)    |                   |                  |
| Lenvatinib                         | 1.29 (0.49-3.52)    | 1.26 (0.39-4.27)     | 0.22 (0.05-0.95)  |                  |
| Sorafenib                          | 1.29 (0.4-4.15)     | 1.25 (0.46-3.52)     | 0.22 (0.06-0.82)  | 1.00 (0.54-1.84) |
| C, Hypertension                    |                     |                      |                   |                  |
| Drug treatment                     | Lenvatinib + TACE   | Sorafenib + TACE     | TACE              | Lenvatinib       |
| Sorafenib + TACE                   | 3.23 (0.63-26.29)   |                      |                   |                  |
| TACE                               | 11.27 (2.05-95.19)  | 3.45 (2.15-5.86)     |                   |                  |
| Lenvatinib                         | 1.07 (0.70-1.63)    | 0.33 (0.04-1.72)     | 0.09 (0.01-0.54)  |                  |
| Sorafenib                          | 1.75 (1.05-2.91)    | 0.54 (0.07-2.91)     | 0.15 (0.02-0.9)   | 1.64 (1.25-2.17) |
| D, Elevated aspartate transaminase |                     |                      |                   |                  |
| Drug treatment                     | Lenvatinib + TACE   | Sorafenib + TACE     | TACE              | Lenvatinib       |
| Sorafenib + TACE                   | 0.69 (0.32-1.48)    |                      |                   |                  |
| TACE                               | 1.14 (0.49-2.63)    | 1.66 (1.22-2.31)     |                   |                  |
| Lenvatinib                         | 8.86 (4.27-20.75)   | 13.04 (6.21-29.34)   | 7.80 (3.47-18.76) |                  |
| Sorafenib                          | 5.07 (2.30-12.01)   | 7.34 (3.89-15.64)    | 4.42 (2.15-10.11) | 0.57 (0.35-0.91) |

| E, Abdominal pain |                   |                    |                   |                  |
|-------------------|-------------------|--------------------|-------------------|------------------|
| Drug treatment    | Lenvatinib + TACE | Sorafenib + TACE   | TACE              | Lenvatinib       |
| Sorafenib + TACE  | 0.69 (0.31-1.50)  |                    |                   |                  |
| TACE              | 1.14 (0.49-2.62)  | 1.66 (1.22-2.30)   |                   |                  |
| Lenvatinib        | 8.88 (4.23-20.39) | 12.96 (6.16-29.46) | 7.84 (3.49-18.62) |                  |
| Sorafenib         | 5.07 (2.28-11.80) | 7.34 (3.83-15.82)  | 4.45 (2.14-10.05) | 0.57 (0.35-0.91) |
| F, Fatigue        |                   |                    |                   |                  |
| Drug treatment    | Lenvatinib + TACE | Sorafenib + TACE   | TACE              | Lenvatinib       |
| Sorafenib + TACE  | 0.68 (0.31-1.46)  |                    |                   |                  |
| TACE              | 1.13 (0.50-2.60)  | 1.66 (1.21-2.3)    |                   |                  |
| Lenvatinib        | 8.83 (4.22-20.66) | 12.98 (6.17-29.91) | 7.81 (3.49-18.78) |                  |
| Sorafenib         | 5.05 (2.28-11.92) | 7.35 (3.84-15.80)  | 4.44 (2.14-10.02) | 0.57 (0.35-0.91) |
| G, Nausea         |                   |                    |                   |                  |
| Drug treatment    | Lenvatinib + TACE | Sorafenib + TACE   | TACE              | Lenvatinib       |
| Sorafenib + TACE  | 0.68 (0.31-1.46)  |                    |                   |                  |
| TACE              | 1.13 (0.50-2.60)  | 1.66 (1.21-2.30)   |                   |                  |
| Lenvatinib        | 8.83 (4.22-20.66) | 12.98 (6.17-29.91) | 7.81 (3.49-18.78) |                  |
| Sorafenib         | 5.11 (2.30-12.05) | 7.38 (3.86-15.73)  | 4.47 (2.14-10.02) | 0.57 (0.35-0.91) |

TACE, transarterial chemoembolization.

**Table SIV.** Results of global inconsistency analysis.

| Intervention              | Deviance Information Criteria |                     | I <sup>2</sup>       |                        |
|---------------------------|-------------------------------|---------------------|----------------------|------------------------|
|                           | Consistency model             | Inconsistency model | Consistency model, % | Inconsistency model, % |
| Overall survival          | 8.989524                      | 12.421999           | 0.0                  | 0.0                    |
| Progression-free survival | 9.067884                      | 9.551256            | 21.0                 | 18.0                   |
| Objective response rate   | 25.122640                     | 26.520960           | 0.0                  | 3.0                    |
| Disease control rate      | 24.904910                     | 26.373670           | 0.1                  | 4.0                    |

The Fixed-effect model was used to reported outcomes. Deviance Information Criteria was adopted to detect global inconsistency. The difference in values of DICs between consistency and inconsistency model were all <1, which indicated that data was consistent. Further, values of I<sup>2</sup><50% indicated no considerable heterogeneity.