

## Supplemental Online Content

Zhou T, Zhang Z, Luo F, et al. Comparison of first-line treatments for patients with extensive-stage small cell lung cancer: a systematic review and network meta-analysis. *JAMA Netw Open*. 2020;3(10):e2015748. doi:10.1001/jamanetworkopen.2020.15748

**eTable 1.** Search Strategy

**eTable 2.** Rank Probabilities With SUCRA Value for Different Outcomes in 5 Kinds of First-line Treatments for Patients With ES-SCLC

**eTable 3.** Evaluation of Inconsistency

**eFigure 1.** Flowchart of Study Selection and Design

**eFigure 2.** Risks of Bias for Included Studies

This supplemental material has been provided by the authors to give readers additional information about their work.

**eTable 1. Search Strategy**

|                        |                                |                                                                                                                                                                                                                                                           |
|------------------------|--------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Small cell lung cancer | #1                             | (((((lung neoplasms[MeSH]) OR "Carcinoma, Small-Cell Lung"[Mesh]) OR lung carcinom*[tiab]) OR lung neoplasm*[tiab]) OR small cell lung cancer[tiab]) OR SCLC[tiab])                                                                                       |
| Extensive stage        | #2                             | (((((("Neoplasm Metastasis"[MeSH]) OR extensive [tiab]) OR stage IV[tiab]) OR stage 4[tiab]) OR metastases[tiab]) OR metastatic[tiab]) OR stage four[tiab]                                                                                                |
| RCT                    | #3                             | ((((((((randomized controlled trial[Publication Type]) OR controlled clinical trial[Publication Type]) OR randomized[tiab]) OR placebo[tiab]) OR drug therapy[sh]) OR randomly[tiab]) OR trial[tiab]) OR groups[tiab]) NOT ((animals[mh]) NOT humans[mh]) |
| Language               | #4                             | English [Language]                                                                                                                                                                                                                                        |
| Date Publication       | #5                             | "2002/01/01"[Date - Publication] : "2019/12/31"[Date - Publication]                                                                                                                                                                                       |
| Search strategy        | #1 AND #2 AND #3 AND #4 AND #5 |                                                                                                                                                                                                                                                           |

**eTable 2. Rank Probabilities With SUCRA Value for Different Outcomes in 5 Kinds of First-line Treatments for Patients With ES-SCLC**

|                                |       |       |       |       |       |                      |
|--------------------------------|-------|-------|-------|-------|-------|----------------------|
| <b>ORR</b>                     |       |       |       |       |       |                      |
| Treatment                      | Rank1 | Rank2 | Rank3 | Rank4 | Rank5 | SUCRA                |
| Etoposide+Platinum             | 0.00  | 0.02  | 0.15  | 0.45  | 0.38  | 0.2025               |
| Etoposide+platinum+Bevacizumab | 0.05  | 0.25  | 0.19  | 0.17  | 0.34  | 0.3750               |
| Etoposide+Platinum+ Ipilimumab | 0.87  | 0.08  | 0.03  | 0.02  | 0.01  | <b><u>0.9500</u></b> |
| Etoposide+Platinum+PD-L1       | 0.05  | 0.29  | 0.26  | 0.19  | 0.21  | 0.4450               |
| Irinotecan+Platinum            | 0.03  | 0.37  | 0.37  | 0.18  | 0.06  | 0.5375               |
| <b>DCR</b>                     |       |       |       |       |       |                      |
| Treatment                      | Rank1 | Rank2 | Rank3 | Rank4 | Rank5 | SUCRA                |
| Etoposide+Platinum             | 0.00  | 0.07  | 0.29  | 0.46  | 0.18  | 0.3125               |
| Etoposide+platinum+Bevacizumab | 0.06  | 0.43  | 0.17  | 0.12  | 0.21  | 0.4975               |
| Etoposide+Platinum+ Ipilimumab | 0.02  | 0.19  | 0.18  | 0.18  | 0.43  | 0.2975               |
| Etoposide+Platinum+PD-L1       | 0.91  | 0.07  | 0.01  | 0.01  | 0.00  | <b><u>0.9700</u></b> |
| Irinotecan+Platinum            | 0.01  | 0.24  | 0.35  | 0.23  | 0.17  | 0.4225               |
| <b>PFS</b>                     |       |       |       |       |       |                      |
| Treatment                      | Rank1 | Rank2 | Rank3 | Rank4 | Rank5 | SUCRA                |
| Irinotecan+Platinum            | 0.13  | 0.36  | 0.34  | 0.16  | 0.01  | 0.6090               |
| Etoposide+Platinum             | 0.00  | 0.00  | 0.02  | 0.15  | 0.83  | 0.0488               |
| Etoposide+Platinum+PD-L1       | 0.12  | 0.33  | 0.33  | 0.18  | 0.03  | 0.5828               |
| Etoposide+Platinum+ Ipilimumab | 0.06  | 0.13  | 0.22  | 0.47  | 0.12  | 0.3856               |
| Etoposide+platinum+Bevacizumab | 0.69  | 0.17  | 0.09  | 0.04  | 0.01  | <b><u>0.8737</u></b> |
| <b>OS</b>                      |       |       |       |       |       |                      |
| Treatment                      | Rank1 | Rank2 | Rank3 | Rank4 | Rank5 | SUCRA                |
| Irinotecan+Platinum            | 0.22  | 0.52  | 0.23  | 0.03  | 0.00  | 0.7331               |
| Etoposide+Platinum             | 0.00  | 0.00  | 0.06  | 0.36  | 0.57  | 0.1246               |
| Etoposide+Platinum+PD-L1       | 0.63  | 0.24  | 0.10  | 0.02  | 0.01  | <b><u>0.8672</u></b> |
| Etoposide+Platinum+ Ipilimumab | 0.03  | 0.06  | 0.24  | 0.39  | 0.27  | 0.2996               |
| Etoposide+platinum+Bevacizumab | 0.12  | 0.17  | 0.36  | 0.19  | 0.16  | 0.4755               |
| <b>TRAE 3-5</b>                |       |       |       |       |       |                      |
| Treatment                      | Rank1 | Rank2 | Rank3 | Rank4 | Rank5 | SUCRA                |
| Etoposide+Platinum             | 0.02  | 0.24  | 0.56  | 0.18  | 0.00  | 0.5250               |
| Etoposide+platinum+Bevacizumab | 0.72  | 0.18  | 0.05  | 0.04  | 0.01  | <b><u>0.8900</u></b> |

|                                |       |       |       |       |                      |                      |
|--------------------------------|-------|-------|-------|-------|----------------------|----------------------|
| Etoposide+Platinum+ Ipilimumab | 0.21  | 0.44  | 0.17  | 0.15  | 0.03                 | 0.6625               |
| Etoposide+Platinum+PD-L1       | 0.05  | 0.13  | 0.20  | 0.59  | 0.04                 | 0.3950               |
| Irinotecan+Platinum            | 0.01  | 0.01  | 0.02  | 0.05  | 0.92                 | 0.0400               |
| <b>Leukopenia</b>              |       |       |       |       |                      |                      |
| Treatment                      | Rank1 | Rank2 | Rank3 | Rank4 | Rank5                | SUCRA                |
| Etoposide+Platinum             | 0.19  | 0.43  | 0.31  | 0.07  | 0.00                 | <b><u>0.6850</u></b> |
| Etoposide+platinum+Bevacizumab | 0.31  | 0.19  | 0.18  | 0.17  | 0.15                 | 0.5850               |
| Etoposide+Platinum+ Ipilimumab | 0.07  | 0.08  | 0.12  | 0.21  | 0.51                 | 0.2425               |
| Etoposide+Platinum+PD-L1       | 0.39  | 0.19  | 0.16  | 0.14  | 0.11                 | 0.6475               |
| Irinotecan+Platinum            | 0.04  | 0.10  | 0.23  | 0.41  | 0.23                 | 0.3325               |
| <b>Neutropenia</b>             |       |       |       |       |                      |                      |
| Treatment                      | Rank1 | Rank2 | Rank3 | Rank4 | Rank5                | SUCRA                |
| Etoposide+Platinum             | 0.34  | 0.45  | 0.19  | 0.03  | 0.00                 | <b><u>0.7800</u></b> |
| Etoposide+platinum+Bevacizumab | 0.33  | 0.23  | 0.25  | 0.16  | 0.03                 | 0.6675               |
| Etoposide+Platinum+ Ipilimumab | 0.13  | 0.11  | 0.20  | 0.39  | 0.17                 | 0.4100               |
| Etoposide+Platinum+PD-L1       | 0.20  | 0.21  | 0.33  | 0.22  | 0.04                 | 0.5775               |
| Irinotecan+Platinum            | 0.00  | 0.00  | 0.03  | 0.20  | 0.76                 | 0.0650               |
| <b>Anemia</b>                  |       |       |       |       |                      |                      |
| Treatment                      | Rank1 | Rank2 | Rank3 | Rank4 | SUCRA                |                      |
| Etoposide+Platinum             | 0.49  | 0.40  | 0.11  | 0.01  | <b><u>0.7933</u></b> |                      |
| Etoposide+Platinum+ Ipilimumab | 0.23  | 0.15  | 0.21  | 0.41  | 0.4000               |                      |
| Etoposide+Platinum+PD-L1       | 0.22  | 0.21  | 0.28  | 0.30  | 0.4533               |                      |
| Irinotecan+Platinum            | 0.06  | 0.24  | 0.41  | 0.28  | 0.3567               |                      |
| <b>Thrombocytopenia</b>        |       |       |       |       |                      |                      |
| Treatment                      | Rank1 | Rank2 | Rank3 | Rank4 | Rank5                | SUCRA                |
| Etoposide+Platinum             | 0.06  | 0.39  | 0.42  | 0.12  | 0.00                 | 0.5925               |
| Etoposide+platinum+Bevacizumab | 0.69  | 0.15  | 0.09  | 0.06  | 0.01                 | <b><u>0.8625</u></b> |
| Etoposide+Platinum+ Ipilimumab | 0.14  | 0.23  | 0.19  | 0.31  | 0.14                 | 0.4850               |
| Etoposide+Platinum+PD-L1       | 0.10  | 0.23  | 0.28  | 0.32  | 0.07                 | 0.4925               |
| Irinotecan+Platinum            | 0.00  | 0.00  | 0.02  | 0.19  | 0.78                 | 0.0575               |
| <b>Diarrhea</b>                |       |       |       |       |                      |                      |
| Treatment                      | Rank1 | Rank2 | Rank3 | Rank4 | Rank5                | SUCRA                |
| Etoposide+Platinum             | 0.00  | 0.00  | 0.05  | 0.35  | 0.60                 | 0.1125               |
| Etoposide+platinum+Bevacizumab | 0.93  | 0.03  | 0.02  | 0.01  | 0.01                 | <b><u>0.9650</u></b> |
| Etoposide+Platinum+ Ipilimumab | 0.04  | 0.44  | 0.27  | 0.15  | 0.10                 | 0.5425               |

|                                |       |       |       |       |       |                      |
|--------------------------------|-------|-------|-------|-------|-------|----------------------|
| Etoposide+Platinum+PD-L1       | 0.01  | 0.10  | 0.21  | 0.39  | 0.29  | 0.2875               |
| Irinotecan+Platinum            | 0.03  | 0.43  | 0.45  | 0.09  | 0.00  | 0.6000               |
| <b>Vomiting</b>                |       |       |       |       |       |                      |
| Treatment                      | Rank1 | Rank2 | Rank3 | Rank4 | Rank5 | SUCRA                |
| Etoposide+Platinum             | 0.00  | 0.11  | 0.35  | 0.43  | 0.10  | 0.3650               |
| Etoposide+platinum+Bevacizumab | 0.30  | 0.22  | 0.17  | 0.20  | 0.11  | 0.6000               |
| Etoposide+Platinum+ Ipilimumab | 0.33  | 0.21  | 0.19  | 0.17  | 0.11  | 0.6250               |
| Etoposide+Platinum+PD-L1       | 0.03  | 0.05  | 0.08  | 0.17  | 0.68  | 0.1500               |
| Irinotecan+Platinum            | 0.34  | 0.41  | 0.21  | 0.04  | 0.00  | <b><u>0.7625</u></b> |
| <b>Nausea</b>                  |       |       |       |       |       |                      |
| Treatment                      | Rank1 | Rank2 | Rank3 | Rank4 | Rank5 | SUCRA                |
| Etoposide+Platinum             | 0.00  | 0.02  | 0.18  | 0.73  | 0.07  | 0.2875               |
| Etoposide+platinum+Bevacizumab | 0.70  | 0.16  | 0.07  | 0.05  | 0.02  | <b><u>0.8675</u></b> |
| Etoposide+Platinum+ Ipilimumab | 0.23  | 0.47  | 0.17  | 0.11  | 0.03  | 0.6950               |
| Etoposide+Platinum+PD-L1       | 0.00  | 0.01  | 0.03  | 0.07  | 0.88  | 0.0400               |
| Irinotecan+Platinum            | 0.07  | 0.34  | 0.55  | 0.04  | 0.01  | 0.6100               |

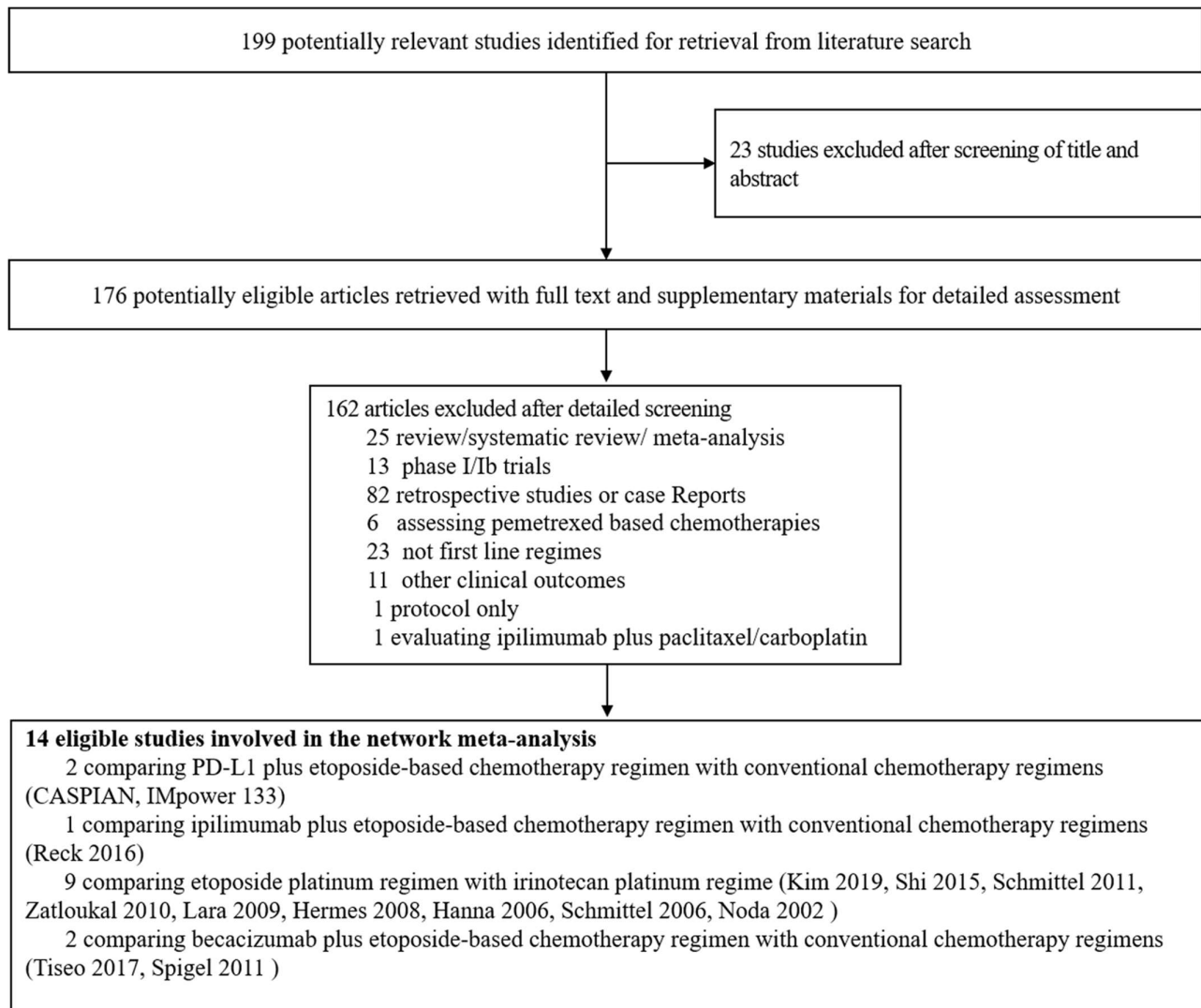
**Abbreviations:** ES-SCLC, extensive stage small cell lung cancer; ORR, objective response rate; DCR, disease control rate; PFS, progression-free survival; OS, overall survival; TRAE 3-5, treatment -related adverse event (grade3-5); SUCRA, surface under the cumulative ranking curve.

**eTable 3. Evaluation of Inconsistency**

| <b>Outcomes</b>         | <b>Random Effects<br/>Standard Deviation<br/>(consistency model)</b> | <b>Random Effects<br/>Standard Deviation<br/>(inconsistency model)</b> | <b>Inconsistency Standard<br/>Deviation(ISD)</b> |
|-------------------------|----------------------------------------------------------------------|------------------------------------------------------------------------|--------------------------------------------------|
| <b>ORR</b>              | 0.32 (0.09, 0.73)                                                    | 0.32 (0.09, 0.71)                                                      | 0.45 (0.02, 0.91)                                |
| <b>DCR</b>              | 0.14 (0.01, 0.65)                                                    | 0.14 (0.01, 0.66)                                                      | 0.43 (0.02, 0.84)                                |
| <b>TRAE3-5</b>          | 0.27 (0.01, 0.89)                                                    | 0.27(0.02, 0.95)                                                       | 0.49 (0.02, 0.95)                                |
| <b>Leukopenia</b>       | 0.82(0.30, 1.50)                                                     | 0.82(0.24, 1.50)                                                       | 0.79(0.04, 1.52)                                 |
| <b>Neutropenia</b>      | 0.69 (0.36, 1.45)                                                    | 0.69 (0.37, 1.46)                                                      | 1.28 (0.07, 2.51)                                |
| <b>Anemia</b>           | 0.51 (0.22, 0.89)                                                    | 0.50 (0.20, 0.89)                                                      | 0.48 (0.03, 0.93)                                |
| <b>Thrombocytopenia</b> | 0.60 (0.22, 1.22)                                                    | 0.60 (0.22, 1.22)                                                      | 0.83 (0.04, 1.61)                                |
| <b>Diarrhea</b>         | 2.15 (1.10, 3.82)                                                    | 2.14 (1.10, 3.82)                                                      | 2.06 (0.11, 3.95)                                |
| <b>Vomiting</b>         | 0.62(0.06, 1.50)                                                     | 0.61(0.05, 1.58)                                                       | 0.80(0.05, 1.58)                                 |
| <b>Nausea</b>           | 0.38(0.04, 1.47)                                                     | 0.33(0.01, 1.42)                                                       | 0.89(0.05, 1.72)                                 |

**Abbreviations:** ORR, objective response rate; DCR, disease control rate; TRAE 3-5, treatment -related adverse event (grade3-5)

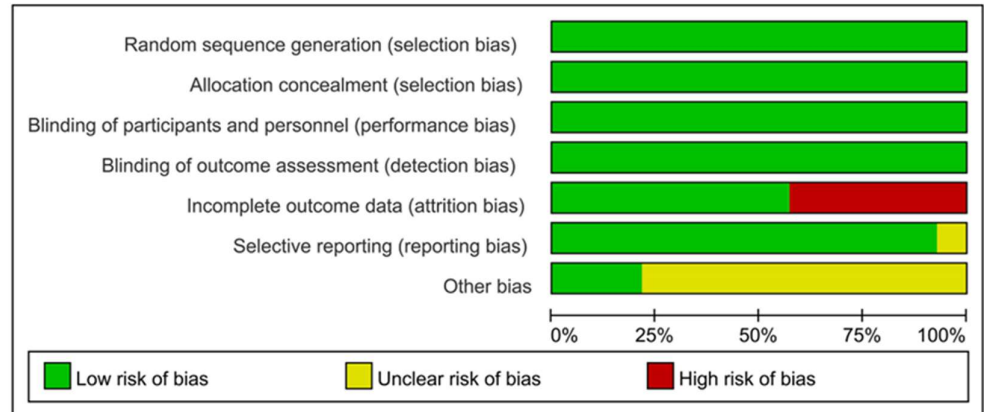
**eFigure 1. Flowchart of Study Selection and Design**



## eFigure 2. Risks of Bias for Included Studies

**Figure S1 Risk of bias for included studies**

**A. Risk of bias graph:** review authors' judgements about each risk of bias item presented as percentages across all included studies



**B. Risk of bias summary:** review authors' judgements about each risk of bias item for each included study

|                                                           | Zaitoukai 2010 | Tiseo 2017 | Spigel 2011 | Shi 2015 | Schmittel 2011 | Schmittel 2006 | Reck 2016 | Noda 2002 | Lara 2009 | Kim 2019 | Impower133 2018 | Hermes 2008 | Hama 2006 | CASPAN 2019 |   |
|-----------------------------------------------------------|----------------|------------|-------------|----------|----------------|----------------|-----------|-----------|-----------|----------|-----------------|-------------|-----------|-------------|---|
| Random sequence generation (selection bias)               | +              | +          | +           | +        | +              | +              | +         | +         | +         | +        | +               | +           | +         | +           | + |
| Allocation concealment (selection bias)                   | +              | +          | +           | +        | +              | +              | +         | +         | +         | +        | +               | +           | +         | +           | + |
| Blinding of participants and personnel (performance bias) | +              | +          | +           | +        | +              | +              | +         | +         | +         | +        | +               | +           | +         | +           | + |
| Blinding of outcome assessment (detection bias)           | +              | +          | +           | +        | +              | +              | +         | +         | +         | +        | +               | +           | +         | +           | + |
| Incomplete outcome data (attrition bias)                  | +              | +          | +           | +        | +              | +              | +         | +         | +         | +        | +               | +           | +         | +           | + |
| Selective reporting (reporting bias)                      | +              | +          | +           | ?        | +              | +              | +         | +         | +         | +        | +               | +           | +         | +           | + |
| Other bias                                                | ?              | +          | ?           | ?        | ?              | ?              | ?         | ?         | ?         | ?        | +               | ?           | ?         | +           | + |