Supplements

Incidence of capillary leak syndrome as an adverse effect of drugs in cancer patients: a systematic review and meta-analysis
Supplementary Table S1. Checklist summarizing compliance with PRISMA guidelines

| Section/topic       | # | Checklist item                                                                                                                                                                                                                                                                                                                                                      | Reported on page # |
|---------------------|---|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
| TITLE               |   |                                                                                                                                                                                                                                                                                                                                                                      |                   |
| Title               | 1 | Identify the report as a systematic review, meta-analysis, or both.                                                                                                                                                                                                                                                                                                   | 1                 |
| ABSTRACT            |   |                                                                                                                                                                                                                                                                                                                                                                      |                   |
| Structured summary  | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.                                                                                             | 3-4               |
| INTRODUCTION        |   |                                                                                                                                                                                                                                                                                                                                                                      |                   |
| Rationale           | 3 | Describe the rationale for the review in the context of what is already known.                                                                                                                                                                                                                                                                                        | 5                 |
| Objectives          | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).                                                                                                                                                           | 5-6               |
| METHODS             |   |                                                                                                                                                                                                                                                                                                                                                                      |                   |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.                                                                                                                                                                                                 | N/A              |
| Eligibility criteria| 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.                                                                                                                                                                                      | 6                 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.                                                                                                                                                                                                 | 6-8               |
| Search              | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.                                                                                                                                                                                                                                           | 6-8               |
| Study selection     | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).                                                                                                                                                                                                                  | 6-8               |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.                                                                                                                                                                                                 | 6-8               |
| Section/topic                  | #   | Checklist item                                                                 | Reported on page # |
|-------------------------------|-----|--------------------------------------------------------------------------------|-------------------|
| Data items                    | 11  | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 6-8               |
| Risk of bias in individual studies | 12  | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | N/A               |
| Summary measures              | 13  | State the principal summary measures (e.g., risk ratio, difference in means).     | 8-9               |
| Synthesis of results          | 14  | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I²), for each meta-analysis. | 8-9               |
| Risk of bias across studies   | 15  | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | N/A               |
| Additional analyses           | 16  | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | N/A               |

### RESULTS

| Section/topic                  | #   | Checklist item                                                                 | Reported on page # |
|-------------------------------|-----|--------------------------------------------------------------------------------|-------------------|
| Study selection               | 17  | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 9 Figure 1        |
| Study characteristics         | 18  | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 9                 |
| Risk of bias within studies   | 19  | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | N/A               |
| Results of individual studies | 20  | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 9-18 Table 1-3, Supplementary figures |
| Synthesis of results          | 21  | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 9-18 Table 1-3, Supplementary figures |
| Category                | Item | Description                                                                 | Page(s) |
|-------------------------|------|-----------------------------------------------------------------------------|---------|
| Risk of bias across studies | 22   | Present results of any assessment of risk of bias across studies (see Item 15). | N/A     |
| Additional analysis   | 23   | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | N/A     |
| DISCUSSION             |      |                                                                             |         |
| Summary of evidence    | 24   | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 19-22   |
| Limitations            | 25   | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 22      |
| Conclusions            | 26   | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 22-23   |
| FUNDING                |      |                                                                             |         |
| Funding                | 27   | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | 24      |

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097
Supplementary Figure S1. Forest plot of meta-analysis to estimate the incidence of capillary leak syndrome according to various anti-cancer treatments.

Supplementary Figure S1(a). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received interleukin-2.

Atkins et al., 1999
Sparano et al., 1993
Tarhini et al., 2007
Talpur et al., 2012
Gallagher et al, 2007
Shusterman et al., 2010
Shaughnessy et al., 2005
Shaughnessy et al., 2005
Frankel et al., 2003
Duvic et al., 2002
Foss et al., 2001
Sievers et al., 2000
Duvic et al., 1998
Meehan et al., 1997
Chang et al., 1993
Carol van et al., 1991
Philip et al., 1989
Carey et al., 1997
Total (fixed effects)
Total (random effects)
Supplementary Figure S1(b). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received interleukin-2 with other agents.

Gallagher et al., 2007
Shaughnessy et al., 2005
Pautier et al., 2013
Pautier et al., 2013
Pautier et al., 2013
O’Brien et al., 2006
Pichert et al., 1991
Sparano et al., 1993
Gilman et al., 2009
Meehan et al., 2010
Yu et al., 2010
Hamblin et al., 1993
Savage et al., 1997
Total (fixed effects)
Total (random effects)
**Supplementary Figure S1(c).** Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received interleukin-2 with interferon-alpha.
Supplementary Figure S1(d). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received interleukin-1 with other agents.
Supplementary Figure S1(e). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received interleukin-2 with imatinib mesylate.
**Supplementary Figure S1(f).** Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received interleukin-2 with bevacizumab.
**Supplementary Figure S1(g).** Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received interleukin-2 and 5-fluorouracil.
Supplementary Figure S1(h). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received GM-CSF.
Supplementary Figure S1(i). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received gemcitabine.
Supplementary Figure S1(j). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received SS1P.
**Supplementary Figure S1(k).** Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received anti-CD agents.

Sausville et al., 1995
Vitetta et al., 1991
Wayne et al., 2014
Amlot et al., 1993
Stathis et al., 2014
Schindler et al., 2011
Bachanova et al., 2015
Schnell et al., 2003
Schnell et al., 2000
Engert et al., 1997
Schnell et al., 2002
Stone et al., 1996
Uckun et al., 1999

Total (fixed effects)
Total (random effects)
Supplementary Figure S1(l). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received anti-CD22 agents.
Supplementary Figure S1(m). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received anti-CD19 + anti-CD22 agents.
Supplementary Figure S1(n). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received anti-CD25 agents.
Supplementary Figure S1(o). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients after bone marrow transplantation (BMT related and drug related).