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	<u>-</u>			
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 Figure 1	
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	

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

Section/topic	#	Checklist item	Reported on page #
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			
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, Supplemen tary figures
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	9-18 Table 1-3, Supplemen tary figures

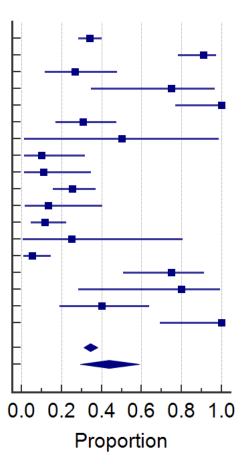
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A	
DISCUSSION				
Summary of evidence	24	Summarize 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

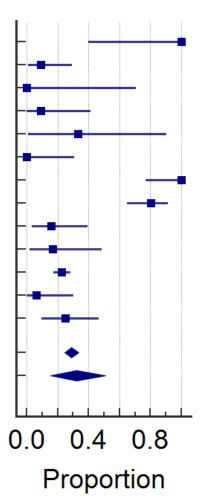
Supplementary Figure S1(a). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received interleukin-2.



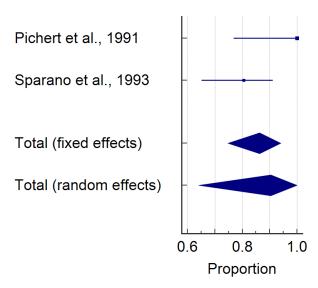


Supplementary Figure S1(b). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received interleukin-2 with other agents.

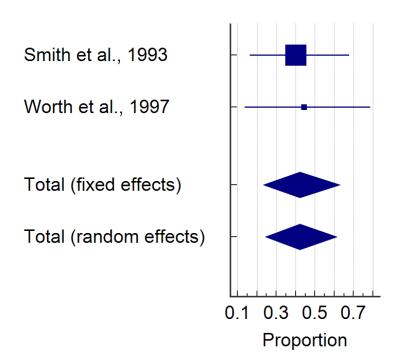
Gallagher et al., 2007 Shaughnessy et al., 2005 Pautier et al., 2013 Pautier et al., 2013 O'Brien et al., 2006 Pichert et al., 1991 Sparano et al., 1993 Gilman et al., 2009 Meehan et al., 2010 Yu et al., 2010 Hamblin et al., 1993 Savage et al., 1997 Total (fixed effects) Total (random effects)



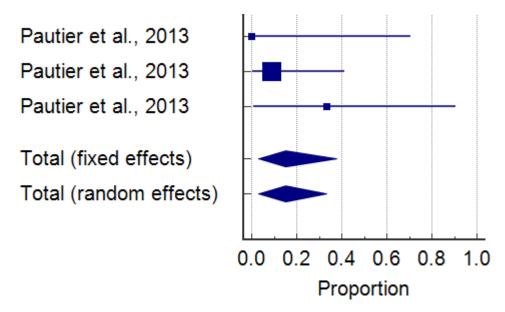
Supplementary Figure S1(c). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received interleukin-2 with interferon-alpha.



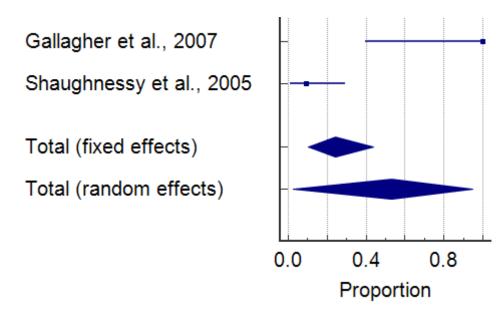
Supplementary Figure S1(d). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received interleukin-1 with other agents.



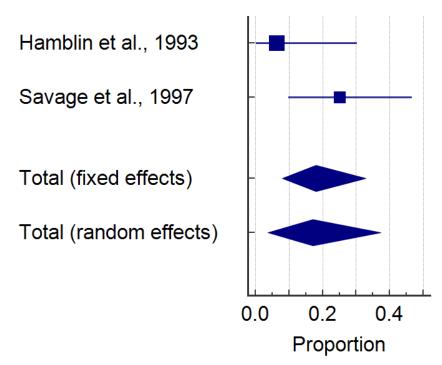
Supplementary Figure S1(e). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received interleukin-2 with imatinib mesylate.



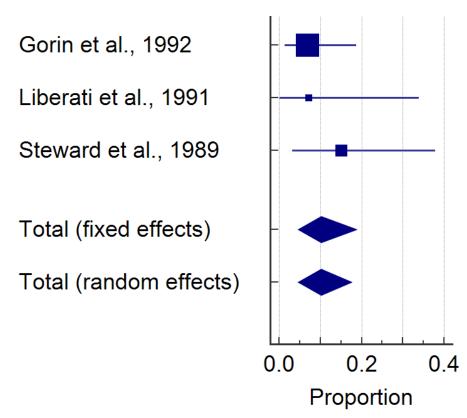
Supplementary Figure S1(f). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received interleukin-2 with bevacizumab.



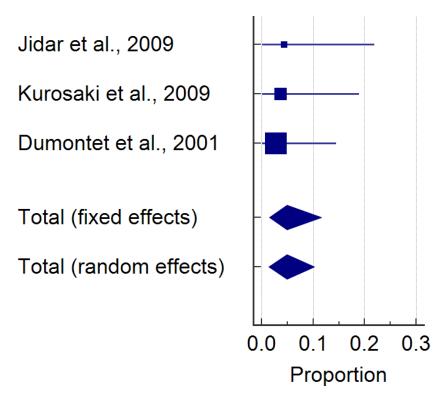
Supplementary Figure S1(g). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received interleukin-2 and 5-fluorouracil.



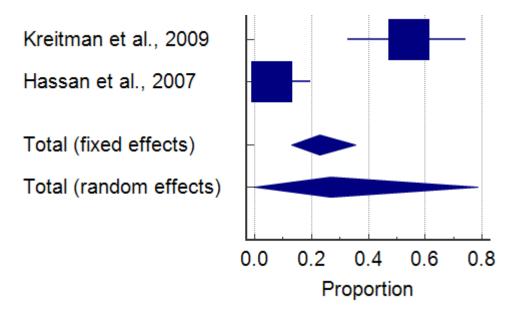
Supplementary Figure S1(h). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received GM-CSF.



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.

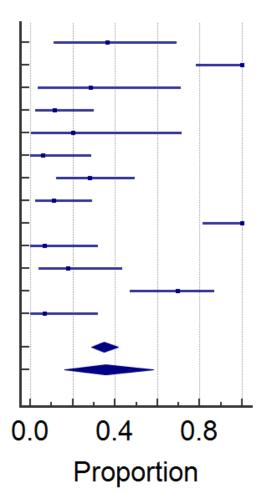


Supplementary Figure S1(j). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received SS1P.

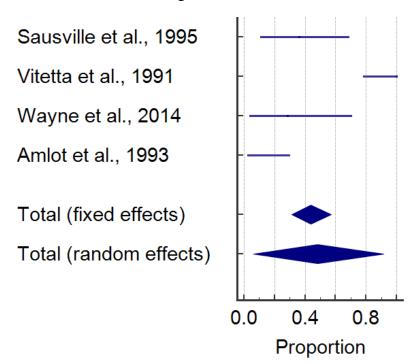


Supplementary Figure S1(k). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received anti-CD agents.

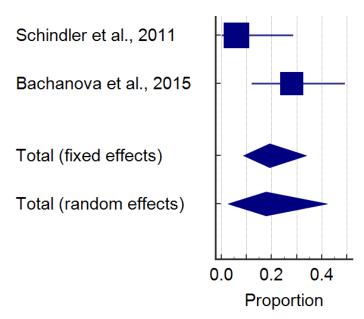
Sausville et al., 1995
Vitetta et al., 1991
Wayne et al., 2014
Amlot et al., 1993
Stathis et al., 2014
Schindler et al., 2011
Bachanova et al., 2015
Schnell et al., 2003
Schnell et al., 2000
Engert et al., 1997
Schnell et al., 1997
Schnell et al., 1996
Uckun et al., 1999
Total (fixed effects)
Total (random effects)



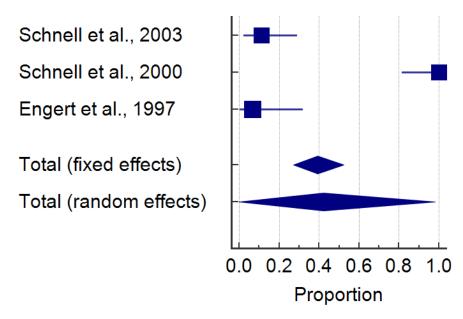
Supplementary Figure S1(l). Forest plot of random effects meta-analysis to estimate the incidence of capillary leak syndrome in cancer patients who received anti-CD22 agents.



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(0). 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).

Cahill, et al., 1996 Nurnberger, et al., 1993 Nurnberger, et al., 1997 Gorin et al., 1992 Steward et al., 1989 Nurnberger, et al., 1997 Salat et al, 1995

Total (fixed effects)
Total (random effects)

