S1 table. The outcomes of studies included in the meta-analysis

Study, Year	participants Total (EH/No EH)*	pCR Total (EH/No EH)*	Complete response Total (EH/No EH)*	Partial response Total (EH/No EH)*	Breast conversion Total (EH/No EH)*	Cardiac ejection fraction decrease more than 10% Total (EH/No EH)*	Cardiac failure Total (EH/No EH)*	Recurrence free survival Total (EH/No EH)*	Overall survival Total (EH/No EH)*
Buzdar et al, 2005	42 (23/19)	20 (15/5)	30 (21/9)	10 (1/9)	23 (13/10)	12 (7/5)	0	41 (23/18)	42 (23/19)
Buzdar et al, 2007	41 (22/19)	17 （12/5）	NR	NR	NR	6 (1/5)	0	38 (22/16)	40 (22/18)
Gianni et al, 2010	235 (117/118)	76 (50/26)	NR	NR	NR	49 (30/19)	2 (2/0)	148 (81/67)	191 (99/92)
Huang et al, 2015	87 (41/46)	38 (20/18)	18 (11/7)	65 (29/36)	2 (NR/NR)	8 (5/3)	0	NR	NR
Yu et al, 2016	58 (29/29)	23 (14/9)	26 (15/11)	16 (9/7)	NR	NR	NR	43 (24/19)	36 (21/15)

EH: the group of concurrent use of trastuzumab(H) and anthracycline(E)-based NAC for HER2-positive breast cancer. **No EH:** the group of non-concurrent use of trastuzumab(H) and anthracycline(E)-based NAC for HER2-positive breast cancer.

S2 table. Quality assessment of the included studies using the Cochrane Collaboration Risk of Bias Assessment Tool

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective bias	Other biases	Aggregate score
Buzdar et al, 2005	*	*	/	*	*	*	?	*****
Buzdar et al, 2007	*	*	/	*	*	*	?	*****
Gianni et al, 2010	*	*	/	*	*	*	?	*****
Huang et al, 2015	*	*	/	*	*	*	?	*****
Yu et al, 2016	*	*	/	*	*	?	?	****

S1 Appendix Data

Search Strategy

1. Pubmed Search strategy

Disease types

1."breast neoplasms"[MeSH Terms]
2."breast neoplasm"[Title/Abstract]
3."breast neoplasms"[Title/Abstract]

4."breast malignancy"[Title/Abstract]
5."breast malignancies"[Title/Abstract]
6."breast malignant"[Title/Abstract]
7."breast cancer"[Title/Abstract]
8."breast cancers"[Title/Abstract]
9."breast tumor"[Title/Abstract]
10."breast tumors"[Title/Abstract]
11."mammary cancer"[Title/Abstract]
12."mammary tumor"[Title/Abstract]
13.or/1-12 (combined all studies)

Interventions
14."doxorubicin"[MeSH Terms]
15."epirubicin"[MeSH Terms]
16."doxorubicin"[Title/Abstract]
17."epirubicin"[Title/Abstract]
18."adriamycin"[Title/Abstract]
19.or/14-18 (combined all studies)

20."trastuzumab"[MeSH Terms]
21."trastuzumab"[Title/Abstract]
22."herceptin"[Title/Abstract]
23.or/20-22 (combined all studies)

24."neoadjuvant"[Title/Abstract]
25."preoperative"[Title/Abstract]

26."preoperation"[Title/Abstract]
27."pretreatment"[Title/Abstract]
28.or/24-27 (combined all studies)

29. and/13,19,23,28 (combined)

2. Embase Search strategy

Disease types
1.'breast cancer'/exp
2.'breast cancer':ab,ti
3.'breast tumor':ab,ti
4.'breast tumors':ab,ti
5.'breast neoplasm':ab,ti
6.'breast malignancy':ab,ti
7.'mammary cancer':ab,ti
8.'mammary tumor':ab,ti
9. or/1-8 (combined all studies)

Interventions
10.'doxorubicin'/exp
11.'doxorubicin':ab,ti
12.'epirubicin':ab,ti
13.'adriamycin':ab,ti
14. or/10-13 (combined all studies)

15.'trastuzumab'/exp
16.'trastuzumab':ab,ti
17.'herceptin':ab,ti
18. or/15-17 (combined all studies)

19.'neoadjuvant':ab,ti
20.'preoperative':ab,ti
21.'preoperation':ab,ti
22.'pretreatment':ab,ti
23. or/19-22 (combined all studies)

24. and/9,14,18,23 (combined)

3. Cochrane Search strategy

Disease types
1. "breast neoplasm":ti,ab,kw
2. "breast malignancy":ti,ab,kw
3. "breast cancer":ti,ab,kw
4. "breast tumor":ti,ab,kw
5. "mammary cancer":ti,ab,kw (Word variations have been searched)
6. or/1-5 (combined all studies)

Interventions
7."doxorubicin":ti,ab,kw
8."epirubicin":ti,ab,kw

9."adriamycin":ti,ab,kw (Word variations have been searched)
10. or/7-9 (combined all studies)

11."trastuzumab":ti,ab,kw
12."herceptin":ti,ab,kw (Word variations have been searched)
13. or/11-12 (combined all studies)

14."neoadjuvant":ti,ab,kw
15."preoperation":ti,ab,kw
16."preoperative":ti,ab,kw
17."pretreatment":ti,ab,kw (Word variations have been searched)
18. or/14-17 (combined all studies)

19. and/6,10,13,18 (combined)

4. Sinomed

Similar search strategy was conducted in Chinese in the Sinomed database.

S1 Appendix File

Section/topic	#	Checklist item	Reported on page #
TITLE			

Title	1	Identify the report as a systematic review, meta-analysis, or both.	Page 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.	Page 1-2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Page 3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Page 3-4
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.	Page 4-5
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.	Page 5
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.	Page 5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Page 5
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).	Page 6
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.	Page 7-8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Page 7-8
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.	Page 7-8

Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Page 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., I^2) for each meta-analysis.	Page 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).	Page 8-9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Page 8-9
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.	Page 6
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.	Page 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).	Page 9
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.	Page 7-10
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Page 9-18
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Page 9-18
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Page 9-18

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).	Page 18-21
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).	Page 21
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Page 22
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.	Page 22

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(7): e1000097. doi:10.1371/journal.pmed1000097

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