Efficacy and safety of PARP inhibitors in the treatment of BRCA-mutated breast cancer: An updated systematic review and meta-analysis of randomized controlled trials

Xiaoyu Sun[1], Suying Xu[1], Yiming Li[2], Xuemei Lv[1], Minjie Wei[1], and Miao He[3]

[1]China Medical University School of Pharmacy
[2]Chinese Academy of Medical Sciences & Peking Union Medical College
[3]Affiliation not available

September 22, 2022

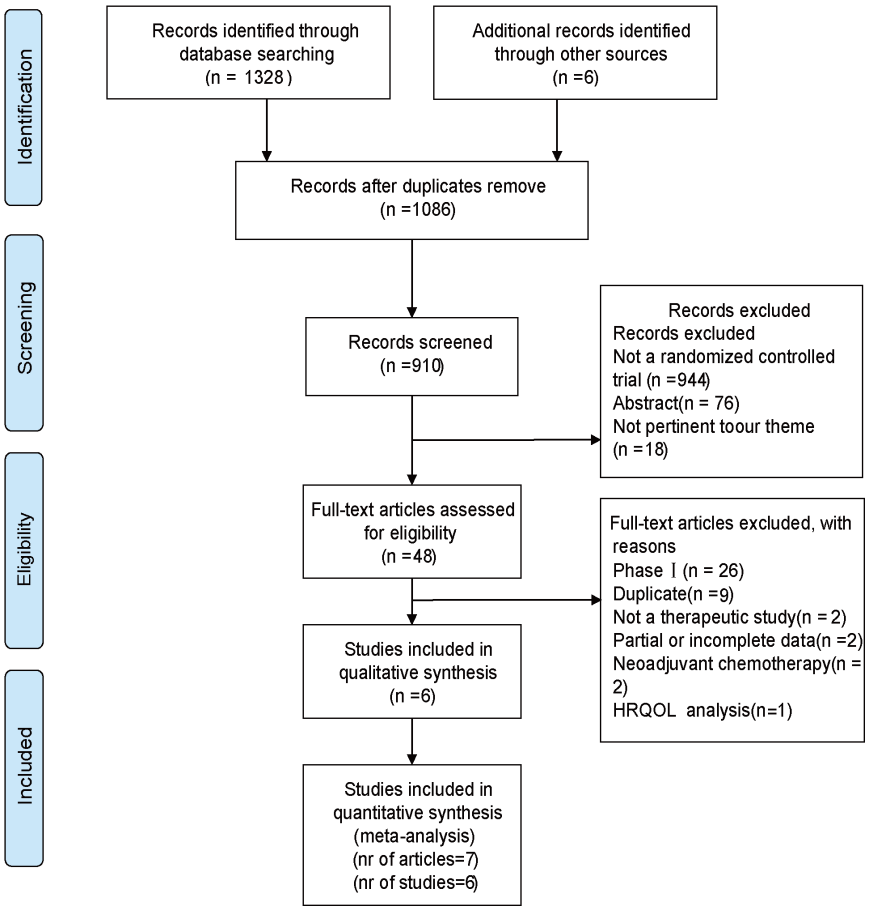
Abstract

Aims: Poly-ADP-ribose polymerase inhibitors have emerged as a new class of therapeutic agents for breast cancer patients with BRCA mutations; however, the efficacy and toxicity of PARP inhibitors have not been clearly established. Methods: This study comprehensively evaluated the efficacy and safety of PARP inhibitors in BRCA mutated breast cancer patients. Online databases were systematically searched, and six clinical trials were included in the meta-analysis. The primary endpoint of efficacy was PFS, secondary endpoints are OS and ORR. In addition, we also assessed safety. Results: The results of the meta-analysis showed that PARP inhibitors can effectively improve the PFS, and OS of patients compared with the control group. The pooled HR (PARP inhibitor vs control group) was 0.63 (95 % CI, 0.55- 0.73) in PFS and 0.83 (95% CI, 0.73 -0.95) in OS among all patients. In terms of safety, PARP inhibitors show controllable adverse reactions. There were no significant differences in overall AEs or grade[?]3 AEs between the PARP inhibitor arms and the control arms. Conclusions: In general, this study demonstrates PARP inhibitors perform well in both monotherapy and combination therapy, not only can provide substantial survival benefit, but also do not increase the additional toxicity burden, and the clinical application is promising.

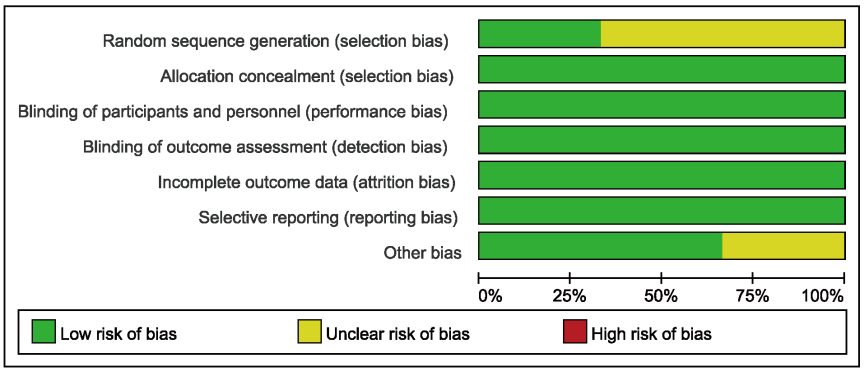
Hosted file

`manusctip--finally.doc` available at https://authorea.com/users/510062/articles/587253-efficacy-and-safety-of-parp-inhibitors-in-the-treatment-of-brca-mutated-breast-cancer-an-updated-systematic-review-and-meta-analysis-of-randomized-controlled-trials

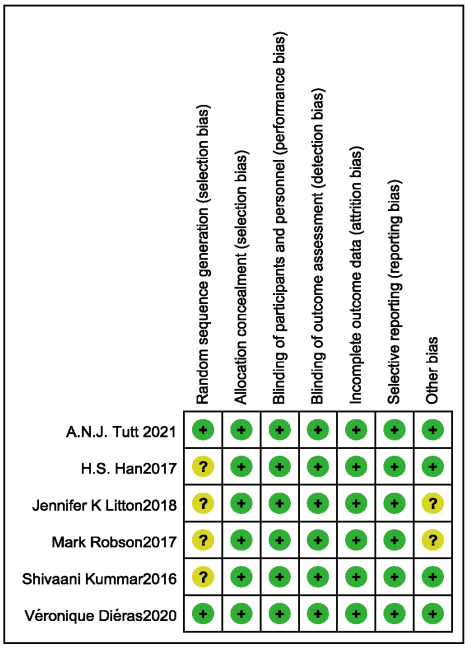
PRISMA 2009 Flow Diagram



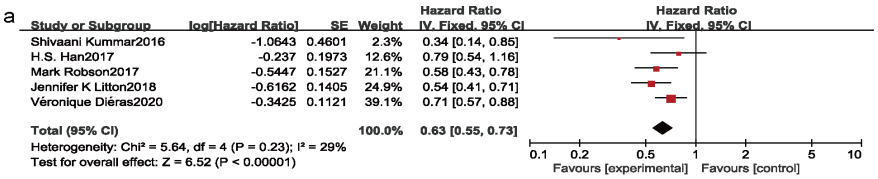
a



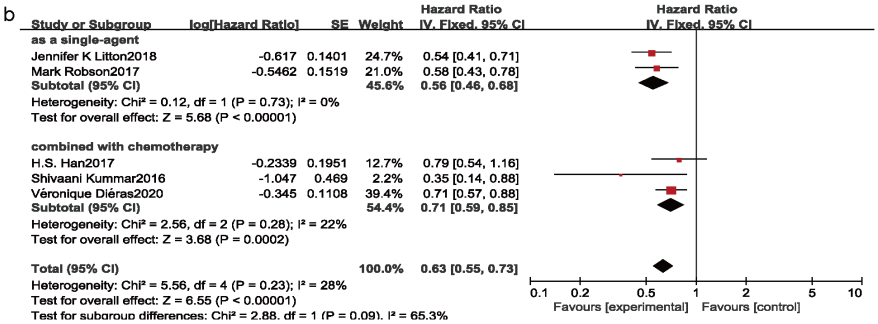
b



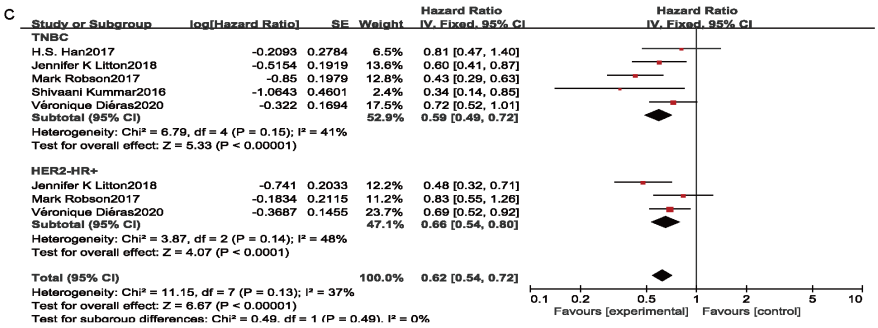
a



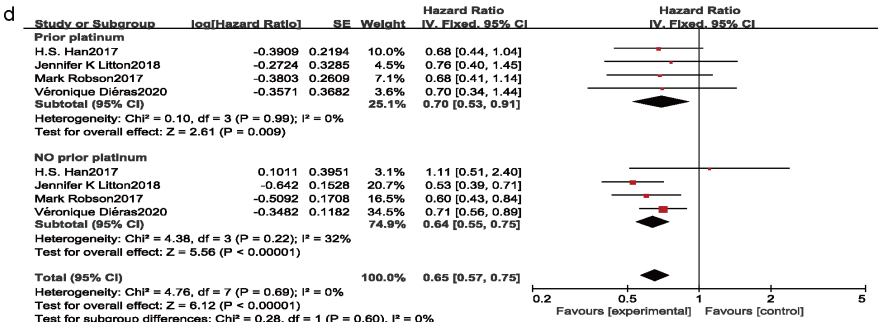
b



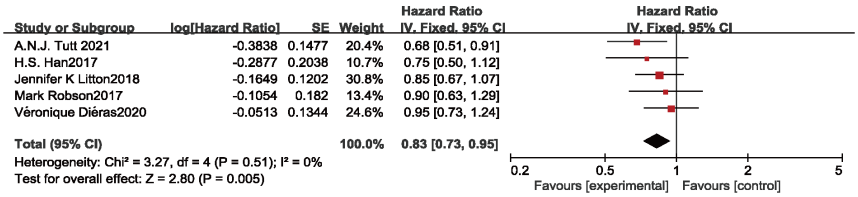
c



d



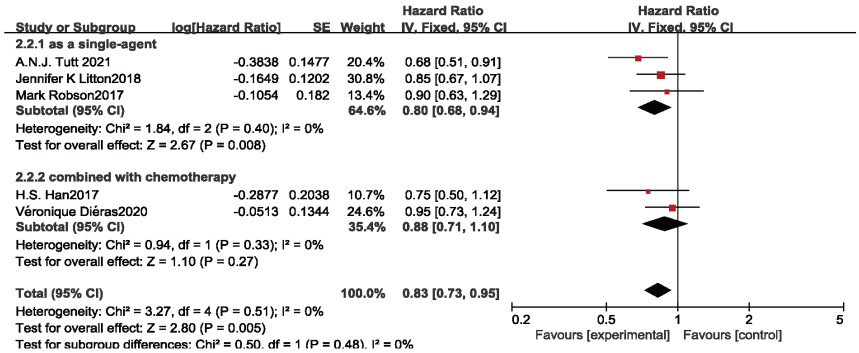
a



Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
A.N.J. Tutt 2021	-0.3838	0.1477	20.4%	0.68 [0.51, 0.91]
H.S. Han2017	-0.2877	0.2038	10.7%	0.75 [0.50, 1.12]
Jennifer K Litton2018	-0.1649	0.1202	30.8%	0.85 [0.67, 1.07]
Mark Robson2017	-0.1054	0.182	13.4%	0.90 [0.63, 1.29]
Véronique Diéras2020	-0.0513	0.1344	24.6%	0.95 [0.73, 1.24]
Total (95% CI)			**100.0%**	**0.83 [0.73, 0.95]**

Heterogeneity: Chi² = 3.27, df = 4 (P = 0.51); I² = 0%
Test for overall effect: Z = 2.80 (P = 0.005)

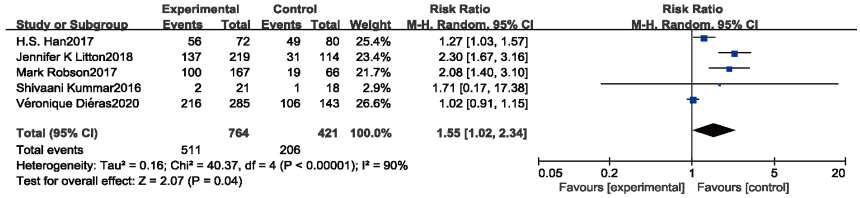
b



Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
2.2.1 as a single-agent				
A.N.J. Tutt 2021	-0.3838	0.1477	20.4%	0.68 [0.51, 0.91]
Jennifer K Litton2018	-0.1649	0.1202	30.8%	0.85 [0.67, 1.07]
Mark Robson2017	-0.1054	0.182	13.4%	0.90 [0.63, 1.29]
Subtotal (95% CI)			**64.6%**	**0.80 [0.68, 0.94]**
2.2.2 combined with chemotherapy				
H.S. Han2017	-0.2877	0.2038	10.7%	0.75 [0.50, 1.12]
Véronique Diéras2020	-0.0513	0.1344	24.6%	0.95 [0.73, 1.24]
Subtotal (95% CI)			**35.4%**	**0.88 [0.71, 1.10]**
Total (95% CI)			**100.0%**	**0.83 [0.73, 0.95]**

Heterogeneity: Chi² = 1.84, df = 2 (P = 0.40); I² = 0%
Test for overall effect: Z = 2.67 (P = 0.008)
Heterogeneity: Chi² = 0.94, df = 1 (P = 0.33); I² = 0%
Test for overall effect: Z = 1.10 (P = 0.27)
Heterogeneity: Chi² = 3.27, df = 4 (P = 0.51); I² = 0%
Test for overall effect: Z = 2.80 (P = 0.005)
Test for subgroup differences: Chi² = 0.50, df = 1 (P = 0.48), I² = 0%

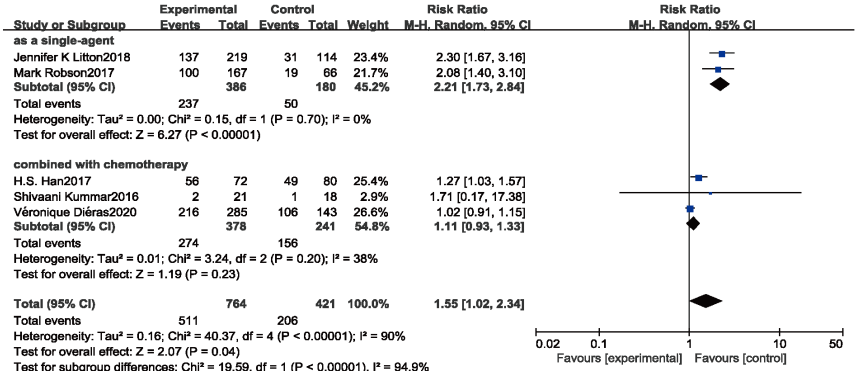
c



Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
H.S. Han2017	56	72	49	80	25.4%	1.27 [1.03, 1.57]
Jennifer K Litton2018	137	219	31	114	23.4%	2.30 [1.67, 3.16]
Mark Robson2017	100	167	19	66	21.7%	2.08 [1.40, 3.10]
Shivaani Kummar2016	2	21	1	18	2.9%	1.71 [0.17, 17.38]
Véronique Diéras2020	216	285	106	143	26.6%	1.02 [0.91, 1.15]
Total (95% CI)		**764**		**421**	**100.0%**	**1.55 [1.02, 2.34]**
Total events	511		206			

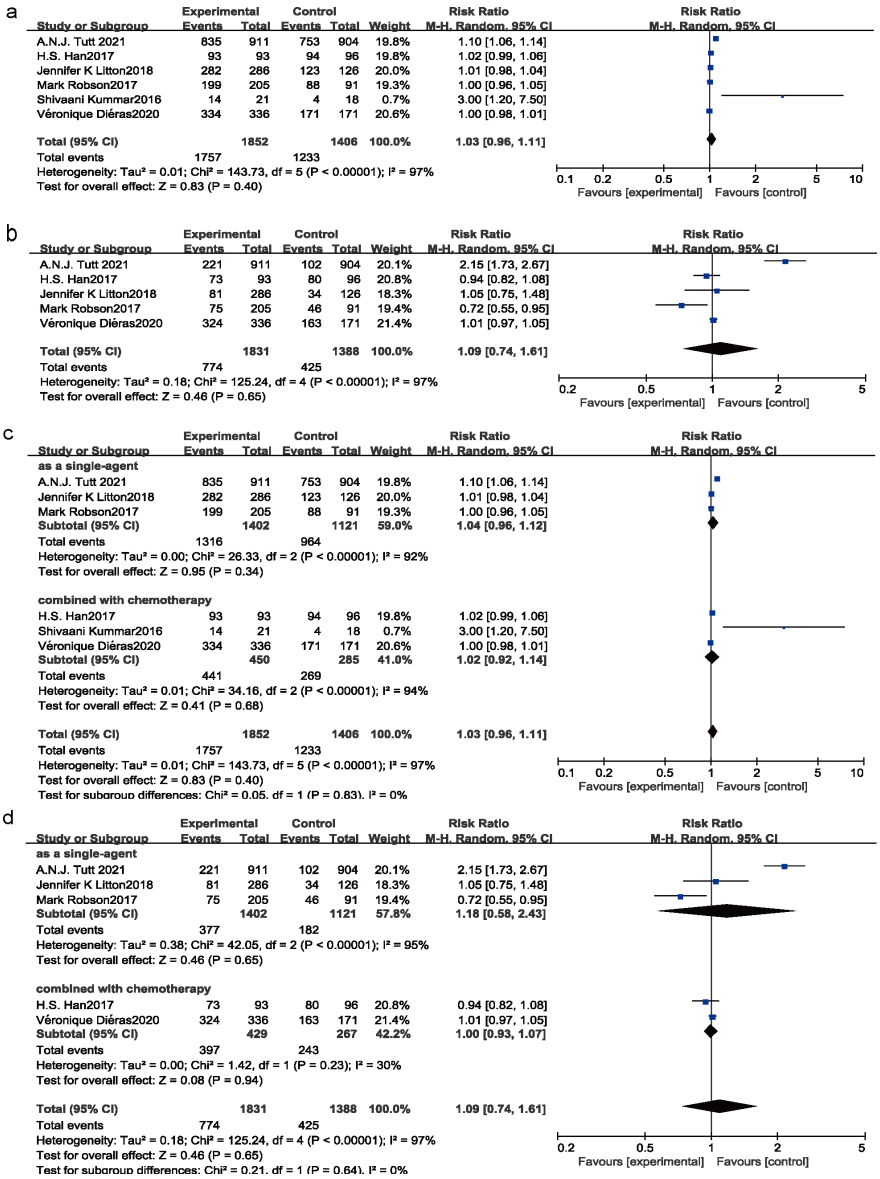
Heterogeneity: Tau² = 0.16; Chi² = 40.37, df = 4 (P < 0.00001); I² = 90%
Test for overall effect: Z = 2.07 (P = 0.04)

d



Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
as a single-agent						
Jennifer K Litton2018	137	219	31	114	23.4%	2.30 [1.67, 3.16]
Mark Robson2017	100	167	19	66	21.7%	2.08 [1.40, 3.10]
Subtotal (95% CI)		**386**		**180**	**45.2%**	**2.21 [1.73, 2.84]**
Total events	237		50			
combined with chemotherapy						
H.S. Han2017	56	72	49	80	25.4%	1.27 [1.03, 1.57]
Shivaani Kummar2016	2	21	1	18	2.9%	1.71 [0.17, 17.38]
Véronique Diéras2020	216	285	106	143	26.6%	1.02 [0.91, 1.15]
Subtotal (95% CI)		**378**		**241**	**54.8%**	**1.11 [0.93, 1.33]**
Total events	274		156			
Total (95% CI)		**764**		**421**	**100.0%**	**1.55 [1.02, 2.34]**
Total events	511		206			

Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 1 (P = 0.70); I² = 0%
Test for overall effect: Z = 6.27 (P < 0.00001)
Heterogeneity: Tau² = 0.01; Chi² = 3.24, df = 2 (P = 0.20); I² = 38%
Test for overall effect: Z = 1.19 (P = 0.23)
Heterogeneity: Tau² = 0.16; Chi² = 40.37, df = 4 (P < 0.00001); I² = 90%
Test for overall effect: Z = 2.07 (P = 0.04)
Test for subgroup differences: Chi² = 19.59, df = 1 (P < 0.00001), I² = 94.9%



Hosted file

Table 1.doc available at https://authorea.com/users/510062/articles/587253-efficacy-and-safety-of-parp-inhibitors-in-the-treatment-of-brca-mutated-breast-cancer-an-updated-systematic-review-and-meta-analysis-of-randomized-controlled-trials

Hosted file

Table 2.doc available at https://authorea.com/users/510062/articles/587253-efficacy-and-safety-of-parp-inhibitors-in-the-treatment-of-brca-mutated-breast-cancer-an-updated-systematic-review-and-meta-analysis-of-randomized-controlled-trials

Hosted file

Table 3.doc available at https://authorea.com/users/510062/articles/587253-efficacy-and-safety-of-parp-inhibitors-in-the-treatment-of-brca-mutated-breast-cancer-an-updated-

systematic-review-and-meta-analysis-of-randomized-controlled-trials

Hosted file

Table 4.docx available at https://authorea.com/users/510062/articles/587253-efficacy-and-safety-of-parp-inhibitors-in-the-treatment-of-brca-mutated-breast-cancer-an-updated-systematic-review-and-meta-analysis-of-randomized-controlled-trials