Search strategy

(BRCA mutation[title] OR PARP inhibitors[title] OR Poly(ADP-ribose) Polymerase Inhibitors[title] OR PARPis[title] OR PARPi[title] OR fluzoparib[title] OR niraparib[title] OR olaparib[title] OR rucaparib[title] OR talazoparib[title] OR iniparib[title] OR veliparib[title]) AND (cancer[title] OR carcinoma[title] OR neoplasm[title] OR leukemia[title] OR lymphoma[title] OR
melanoma[title] OR malignancy[title] OR malignancies[title] OR tumor[title] OR
tumors[title]) AND (versus[title/abstract] OR vs[title/abstract] OR compare[title/abstract] OR comparison[title/abstract] OR comparative[title/abstract] OR comparing[title/abstract] OR trial[title/abstract] OR phase[title/abstract]) AND (English[Language]) AND ("2009/01/01"[Date - Publication]:"2020/02/19"[Date - Publication])

Table S1 Quality assessment of the 14 studies for Bayesian network meta-analysis*

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias	Overall	Modified Jadad score†
Mansoor Raza Mirza, 2019	low	low	high	high	low	low	low	high	5
Jennifer K. Litton, 2018	low	low	high	low	low	low	low	high	4
Mark Robson, 2017	low	low	high	low	low	low	low	high	5
Joyce F Liu, 2019	low	low	high	high	low	low	low	high	5
Robert L Coleman, 2017	low	low	low	low	low	low	low	low	7
Stan B. Kaye, 2011	low	low	high	high	low	low	low	high	5
A. González-Martín, 2019	low	low	low	low	low	low	low	low	6
Mansoor R. Mirza, 2016	low	unclear	low	low	low	low	low	unclear	6
Jonathan Ledermann, 2012	low	low	low	low	low	low	low	low	7
K. Moore, 2018	low	low	low	low	low	low	low	low	7
Eric Pujade-Lauraine, 2017	low	low	low	low	low	low	low	low	7
Richard T. Penson, 2020	low	low	high	low	low	low	low	high	5
Joaquin Mateo, 2020	low	low	high	high	low	low	low	high	5
Talia Golan, 2019	low	low	low	low	low	low	low	low	7

*Quality assessment was based on the original study, possible updated study and supplementary materials, but not study protocol. †Modified Jadad scale rates the adequacy of generation of random sequence, allocation concealment, blinding method, and drop out/loss of follow-up; high-quality study had a score ≥ 4; low-quality, ≤ 3.

https://dx.doi.org/10.21037/atm-21-1883

Table S2 Nodesplit analysis of the dosage-based network meta-analysis

Nodes	Direct effect	Indirect effect	Overall	P*
Grade ≥3 AEs				
CT, olaparib-1	1.2(0.72 to 2.0)	0.78(0.15 to 3.8)	1.2(0.72 to 1.9)	0.60355
placebo, olaparib-1	0.38(0.24 to 0.61)	0.59(0.19 to 1.8)	0.41(0.27 to 0.62)	0.4638
olaparib-3, olaparib-1	1.2(0.44 to 3.1)	0.95(0.45 to 2.2)	1.0(0.59 to 1.9)	0.72245
olaparib-3, CT	1.3(0.31 to 5.4)	0.79(0.36 to 1.9)	0.88(0.45 to 1.8)	0.57945
olaparib-3, placebo	2.1(1.0 to 4.8)	3.3(1.3 to 8.3)	2.5(1.5 to 4.5)	0.46055

AE: adverse events. olaparib-1: olaparib (300mg). olaparib-3: olaparib (400mg). CT: conventional therapy. * P ≤ 0.05 indicates a significant inconsistency between the direct effect and indirect effects.

niraparib	**0.29** (0.105, 0.787)	**0.245** (0.134, 0.442)	0.762 (0.342, 1.673)	**0.286** (0.132, 0.591)	**0.099** (0.064, 0.155)	2.29 (0.891, 5.991)	0.278 (0.054, 1.557)	**0.251** (0.125, 0.526)
3.452 (1.271, 9.555)	talazoparib	0.843 (0.37, 1.951)	2.632 (0.857, 8.092)	0.989 (0.497, 1.958)	**0.343** (0.139, 0.855)	**7.919** (1.991, 31.747)	0.962 (0.185, 5.27)	0.87 (0.332, 2.376)
4.086 (2.262, 7.481)	1.186 (0.513, 2.7)	olaparib-1	**3.1** (1.445, 6.876)	1.17 (0.721, 1.865)	**0.407** (0.271, 0.613)	**9.353** (3.115, 29.581)	1.132 (0.243, 5.671)	1.031 (0.582, 1.868)
1.312 (0.598, 2.922)	0.38 (0.124, 1.167)	**0.323** (0.145, 0.692)	rucaparib	**0.377** (0.15, 0.899)	**0.131** (0.067, 0.254)	3.004 (0.889, 10.47)	0.365 (0.064, 2.166)	**0.331** (0.139, 0.807)
3.498 (1.691, 7.55)	1.011 (0.511, 2.011)	0.854 (0.536, 1.388)	**2.652** (1.112, 6.646)	conventional therapy	**0.347** (0.194, 0.647)	**8.012** (2.445, 27.116)	0.974 (0.224, 4.574)	0.88 (0.45, 1.792)
10.068 (6.469, 15.684)	**2.917** (1.17, 7.182)	**2.458** (1.63, 3.693)	**7.627** (3.944, 14.956)	**2.882** (1.547, 5.168)	placebo	**23.073** (8.169, 66.781)	2.796 (0.573, 14.35)	**2.528** (1.444, 4.53)
0.437 (0.167, 1.122)	**0.126** (0.031, 0.502)	**0.107** (0.034, 0.321)	0.333 (0.096, 1.125)	**0.125** (0.037, 0.409)	**0.043** (0.015, 0.122)	PARPi+AI	**0.121** (0.018, 0.853)	**0.11** (0.033, 0.365)
3.592 (0.642, 18.456)	1.039 (0.19, 5.415)	0.883 (0.176, 4.117)	2.74 (0.462, 15.561)	1.027 (0.219, 4.473)	0.358 (0.07, 1.746)	**8.254** (1.173, 55.611)	olaparib-2	0.908 (0.167, 4.681)
3.979 (1.902, 8.023)	1.15 (0.421, 3.009)	0.97 (0.535, 1.717)	**3.025** (1.239, 7.174)	1.136 (0.558, 2.22)	**0.396** (0.221, 0.692)	**9.052** (2.741, 30.372)	1.102 (0.214, 5.985)	olaparib-3

Figure S1 Safety profile according to the dosage-based NMA results in the consistency model. Each cell of the safety profile contains the pooled odds ratios and 95% confidence intervals for grade 3-5 adverse events; significant results are in bold. PARPi+AI: one PARP inhibitor with one angiogenesis inhibitor; olaparib-1: olaparib 300mg twice daily; olaparib-2: olaparib 200 mg twice daily; olaparib-3: olaparib 400 mg twice daily. PARPi, poly (ADP-ribose) polymerase inhibitor; AI, angiogenesis inhibitor.

https://dx.doi.org/10.21037/atm-21-1883

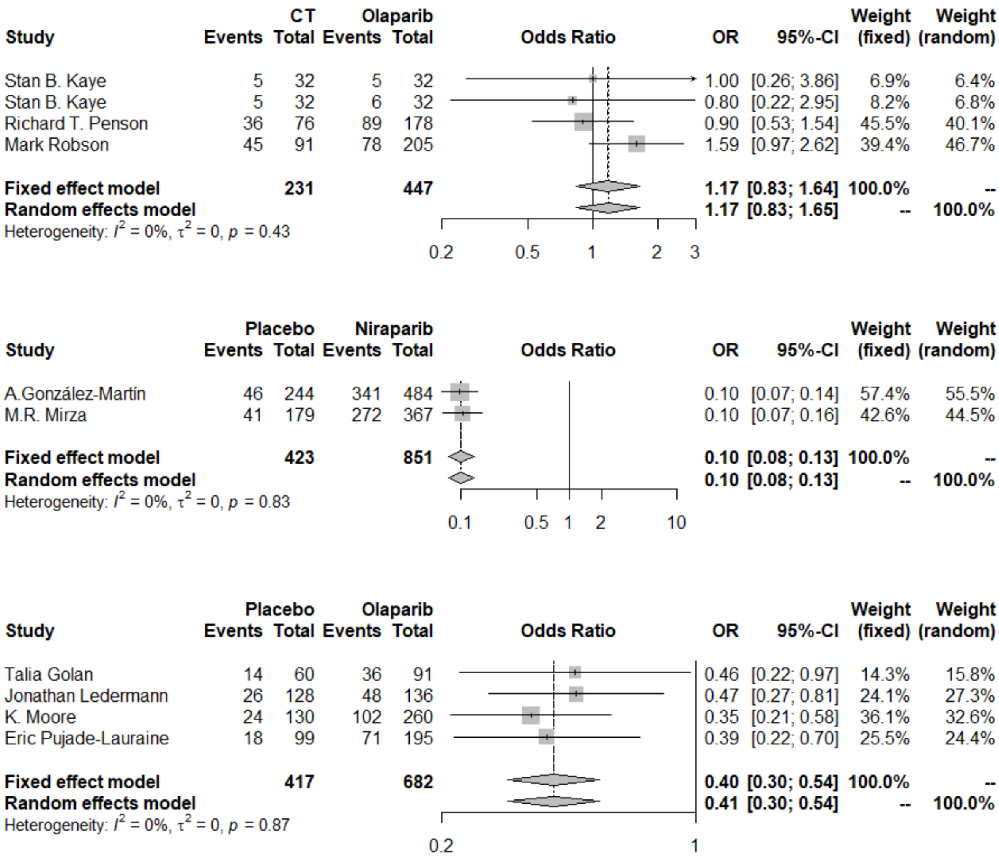

Figure S2 Forest plots and PWMA of head-to-head comparisons for the risk of grade 3-5 adverse events. Squares are the point estimates of the odds ratios with the 95% CIs indicated by horizontal bars. Diamonds are the summary estimates and 95% CIs from the pooled studies. PWMA: pairwise meta-analysis. CIs: confidence intervals. CT: conventional therapy.

Table S3 Detailed rank and probability in the category-based network meta-analysis

Treatment	Rank probability*						
	1	2	3	4	5	6	7
Grade ≥3 AEs							
niraparib	0	0	0	0	20	77	3
talazoparib	1	29	22	45	3	0	0
olaparib	0	57	27	15	0	0	0
rucaparib	0	0	0	3	75	19	3
CT	0	12	50	37	0	0	0
placebo	99	1	0	0	0	0	0
PARPi+AI	0	0	0	0	2	4	94

AE: adverse events. CT: conventional therapy. PARPi: poly (ADP-ribose) polymerase inhibitor; AI: angiogenesis inhibitor. *preferred direction = -1. Values are presented as probability (%).

https://dx.doi.org/10.21037/atm-21-1883

Table S4 Sensitivity analysis

Groups	Rank probability*						
	1	2	3	4	5	6	7
Phase III studies							
Grade ≥3 AEs							
niraparib	0	0	0	2	23	74	–
talazoparib	2	25	24	41	6	2	–
olaparib	0	61	24	14	1	0	–
rucaparib	0	1	2	5	68	23	–
CT	0	11	48	38	2	0	–
placebo	97	2	0	0	0	0	–
Studies explicitly reporting grade ≥ 3 AEs							
Grade ≥3 AEs							
niraparib	0	0	0	1	21	74	3
talazoparib	1	25	25	44	4	1	0
olaparib	0	63	24	13	0	0	0
rucaparib	0	0	1	4	72	20	3
CT	0	10	49	39	1	0	0
placebo	98	1	0	0	0	0	0
PARPi+AI	0	0	0	0	2	5	93
Studies using the current recommended dosage of PARPi							
Grade ≥3 AEs							
niraparib	0	0	0	1	21	73	4
talazoparib	2	25	24	41	5	2	1
olaparib	0	61	25	14	1	0	0
rucaparib	0	1	2	5	68	20	4
CT	0	11	47	39	2	1	0
placebo	97	2	1	0	0	0	0
PARPi+AI	0	0	0	0	2	5	92

AE: adverse events. CT: conventional therapy. PARPi: poly (ADP-ribose) polymerase inhibitor; AI: angiogenesis inhibitor. *preferred direction = -1. Values are presented as probability (%).

https://dx.doi.org/10.21037/atm-21-1883