Efficacy and safety analysis of PARP inhibitors combined with drugs for primary and relapsed ovarian cancer: A meta-analysis of randomized controlled trials

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July 18, 2022

Abstract

Background: Poly ADP-ribose polymerase (PARP) inhibitors have emerged as maintenance therapy for advanced ovarian cancer. However, due to the development of drug resistance, combination of PARP inhibitors with other chemotherapeutic agents has become a contemporary research hotspot. Methods: We conducted a meta-analysis of phase II or III randomized controlled trials to analyze the efficacy and safety of combinations of PARP inhibitors with various chemotherapeutic agents on the progression-free survival (PFS) and overall survival (OS) of patients with ovarian cancer. Results: A total of eight trials that contained the combination of PARP inhibitors and chemotherapeutic agents were included. Combination of PARP inhibitors with bevacizumab benefited patients with BRCA mutations and HRD-positive status(HR=0.34 (95% Cl: 0.23–0.5; P<0.05); HR=0.35 (95% Cl: 0.27–0.45; P<0.05)), while combination with chemotherapy prolonged the PFS in the BRCA mutation, HRD, and homologous recombination proficiency subgroups(HR=0.39 (95% Cl: 0.26–0.58; P<0.05);HR=0.57 (95% Cl: 0.43–0.76; P<0.05); HR=0.79 (95% Cl: 0.64–0.98; P<0.05)). However, patients with BRCA wild-type or unknown type benefited most from combination with cediranib. PARP inhibitors increased the risk of G[?]3 neutropenia when combined with bevacizumab(RR=2.25, 95% Cl 1.09–4.62; P<0.05) and G[?]3 anemia(RR=1.54, 95% Cl 1.16–2.05; P<0.05) and neutropenia(RR=1.25,95% CL 1.00-1.57; P<0.05) when combined with chemotherapy. Conclusion: Combination regimens of PARP inhibitors showed benefits in both primary and recurrent ovarian cancer, and the population subsets benefiting varied among different combinations. G[?]3 adverse reactions were mainly hematological toxicities.

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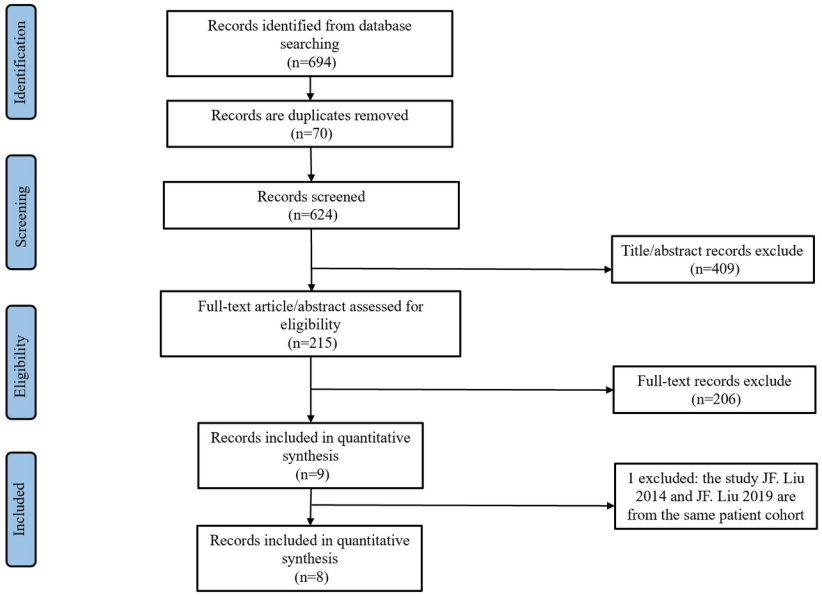

FIGURE 1 | Flow diagram of study inclusion and exclusion

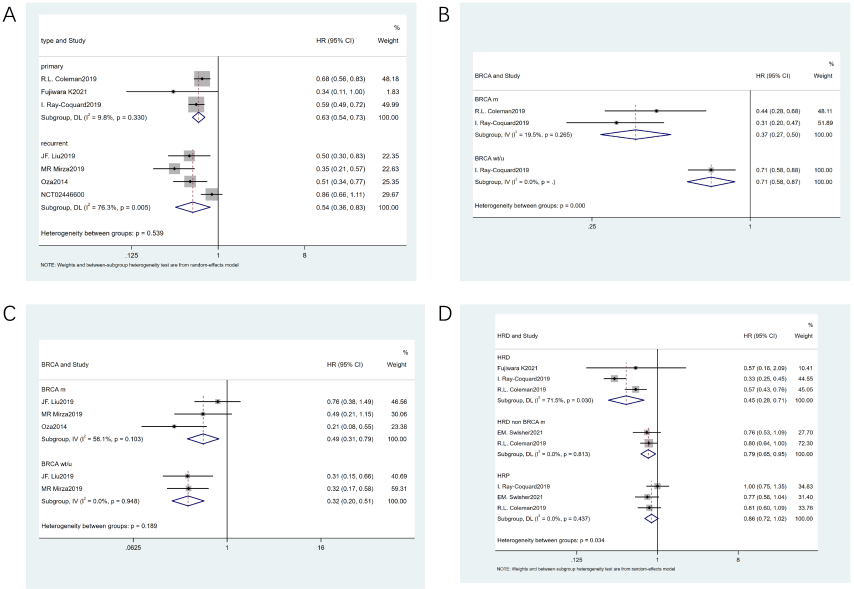

FIGURE 2| forest plots of pooled analyses for the effect of PARP inhibitors combination agents on P PFS in (A)intention to treat (B)BRCA m vs.BRCAwt/u on primary OC (C)BRCAm vs.BRCAwt/u on recurrent OC(D)HRD positive vs.HRD negtive on primary OC

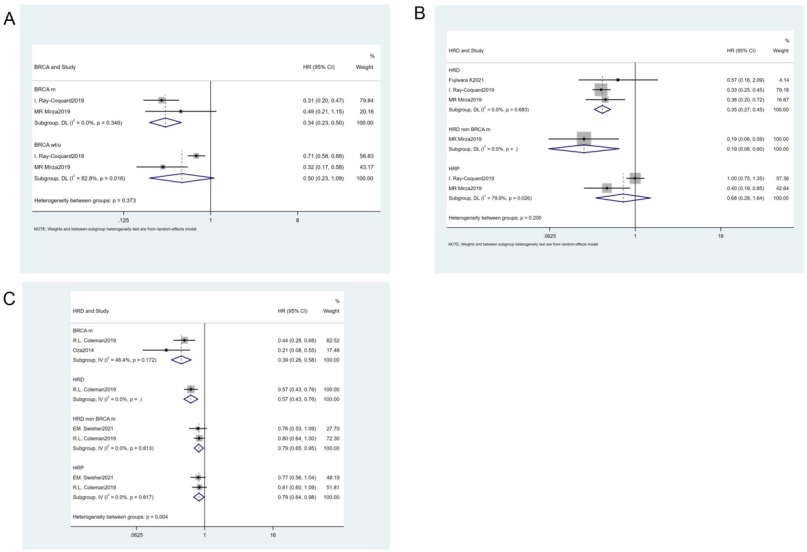

FIGURE 3 | Forest plots of pooled analyses for the effect of diverse PARP inhibitors combination agents on PFS in (A) BRCA status on combination of bevacizumab (B) HRD status on combination of bevacizumab (C) combination of chemotherapy

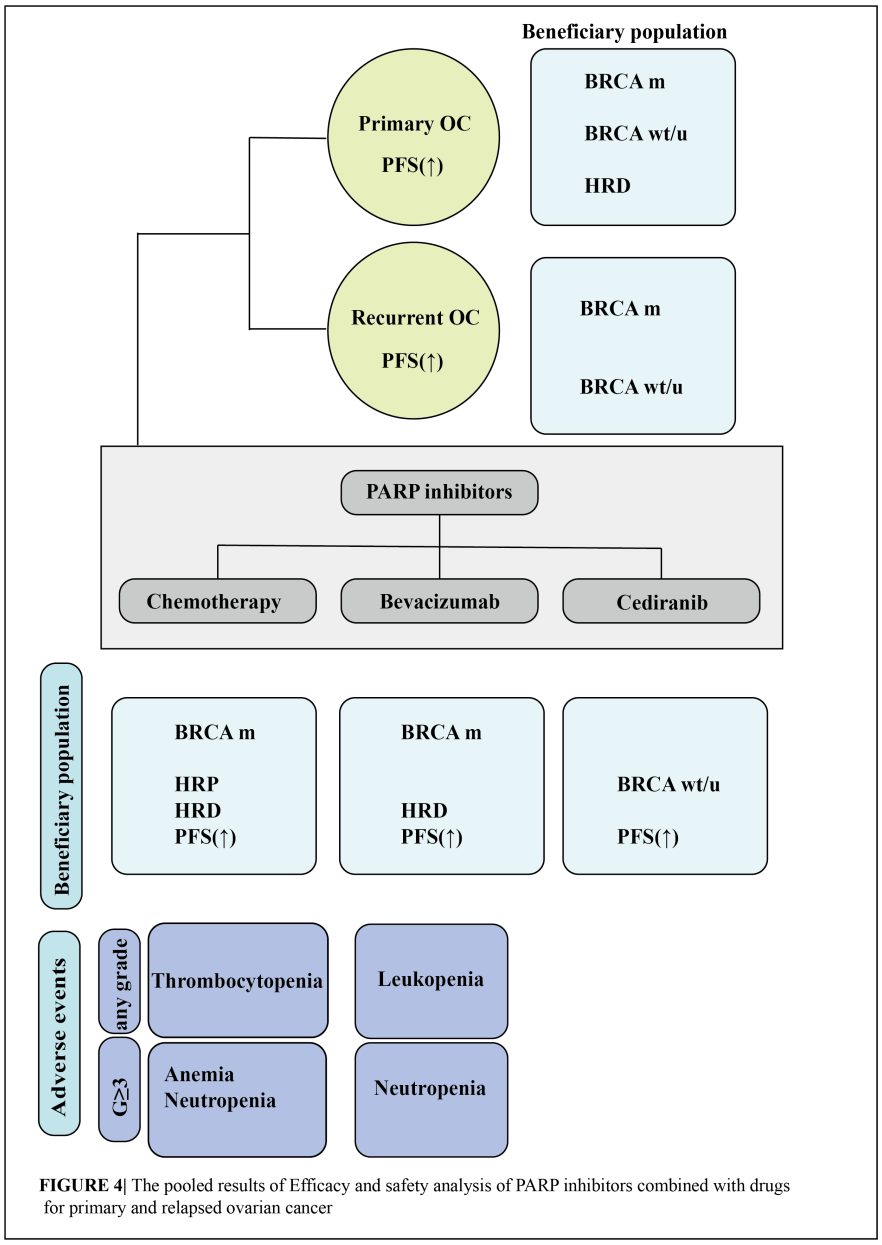

FIGURE 4| The pooled results of Efficacy and safety analysis of PARP inhibitors combined with drugs for primary and relapsed ovarian cancer

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