Risk of fatigue and neuropathy in patients with advanced cancer treated with olaparib: A meta-analysis of randomized controlled trials

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Background: Poly ADP ribose polymerase (PARP) inhibitors are a new class of drugs that are currently being studied in several malignancies. Olaparib is FDA-approved for patients with advanced breast cancer and advanced ovarian cancer. Fatigue is the most common symptom associated with advanced cancer and treatment. Neuropathy is also a treatment-related adverse event associated commonly with platinum and taxanes. We did a systematic and up-to-date review of the literature and a meta-analysis of randomized controlled trials (RCTs) to characterize the risk of fatigue and neuropathy associated with olaparib use.

Methods: PubMed databases were searched for articles published till February 2018. The search was restricted to randomized controlled trials (RCTs) with olaparib and were selected according PRISMA. Safety profiles from each selected study was evaluated for all-grade and high-grade fatigue and neuropathy events in control/placebo and olaparib arms. Summary incidences and the relative risk (RR), with 95% confidence intervals, of all-grade and high-grade events were calculated using random-effects or fixed-effects model based on the heterogeneity of selected studies.

Results: A total of 7 trials were selected, and included a total of 1750 patients with advanced ovarian, gastric or breast cancer. 746 patients received placebo/control treatments and 1004 received olaparib alone or in association with control. All-grade fatigue was increased by 21% (HR 1.21; 95% CI 1.07-1.37) while all-grade neuropathy was increased by 59% (HR 1.55; 95% CI 1.35-1.80). High-grade fatigue analysis showed a HR of 1.64 (95% CI 0.98-2.77) and high-grade neuropathy a HR of 3.61 (95% CI 0.60-21.85).

Conclusions: Our findings suggest that the olaparib treatment is associated with an increased risk of fatigue and neuropathy adverse events. Since fatigue and neuropathy are very common treatment-related adverse events, and both can impair the quality of life of patients, it is important to identify it early and manage it accordingly in order to optimize the overall treatment.

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