Letter to the Editor

Is gemcitabine (GEM)-based combination therapy good for the treatment of advanced pancreatic cancer?

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With great interest, we carefully read the recent paper by Dr. Zhang and colleagues published in *Journal of Gastrointestinal Oncology* (1).

Chemotherapy is used widely in the treatment of patients with advanced pancreatic cancer (PC). As a synthetic analog of cytarabine, gemcitabine (GEM) is one of the most used chemotherapeutic drugs for PC. Many attempts have been made to increase the overall survival of patients with PC, in particular, by exploring the combination of GEM with other drugs. GEM-based chemotherapy was proposed as a standard therapy treatment for patients with unresectable PC. The study by Zhang *et al.* (1) which included 17 studies with a total of 5,197 patients, revealed that comparing with GEM alone, GEM-based combination therapy has better efficacy for advanced PC. Although GEM-based combination therapy can improve the overall survival, progression-free survival and overall response rate, there are more adverse events. Our aim with this letter is to address some shortcomings in this study.

First of all, the investigators did not describe search strategy in detail for the eight databases. They just provided some key words to search feasible studies that may not find all of the articles related to this topic. Accordingly, we suggest that the authors provided a complete search strategy in supplementary materials to make this study more robust. Although, the authors claimed that this study was adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) standards, after careful review, we found that this system review didn't provide the registration information in The International Prospective Register of Systematic Reviews (PROSPERO) and no central registration depository (CRD) number (2). Furthermore, according to the Cochrane Collaboration's risk of bias tool, the study should provide quality assessment for the included literature with detailed scores, and not just defined them as low risk ('good' quality) with 6–8 points, unclear risk ('moderate' quality) with 3–5 points, and high risk ('poor' quality) with 0–2 points.

Second, although the authors claimed that the all included studies in this study are randomized controlled trials (RCTs), after carefully reading, we found that the reference 23 is a retrospective study (3). What's more, according to the inclusion criteria of this study, only patients with advanced PC can be included. With a close examination of the manuscript, we found that the patients are with resectable PC in reference 35 (4). And some studies included unresectable PC and locally advanced and/or metastatic pancreatic carcinoma like references 27 and 30 (5,6). We suggest that the authors define the definition of advanced PC clearly.

Third, it is suggested that the author should include patients with the same pathological type of PC for comparison, because different pathological types of PC have different responses to GEM, may result in some bias. We urgently want to know whether the included patients with PC undergo chemotherapy after surgery, because the survival time of patients undergoing chemotherapy after surgery is significantly different from those patients undergoing direct chemotherapy.

In conclusion, thank all authors for their excellent

contributions to assess the efficiency of GEM-based combination therapy. In our opinion, further high quality RCTs are still needed to further validate these findings.

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