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【 LETTERS TO THE EDITOR 】

Response to the Letter to the Editor 'Reply to "Clinical Safety and Efficacy of Secondary Prophylactic Pegylated G-CSF in Advanced Pancreatic Cancer Patients Treated with mFOLFIRINOX: A Single-center Retrospective Study" by Dr. Peng Chen'

Key words: pegylated G-CSF, mFOLFIRINOX, pancreatic cancer

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The Authors Reply We thank Dr. Chen et al. for their interest in our article, in which we assessed the clinical efficacy and safety of modified FOLFIRINOX (mFOLFIRINOX) combined with secondary prophylaxis using Pegylated granulocyte colony-stimulating factor (Peg G) in advanced pancreatic cancer patients (1). They raised several concerns regarding our study.

First, Dr. Chen et al. pointed out that the incidence of grade 3 or 4 anorexia and nausea was lower in our study than in a previous study in which pancreatic cancer patients were treated with FOLFIRINOX combined with primary prophylaxis using Peg G (2). Thus, the incidence of these non-hematological toxicities accompanied by mFOLFIRINOX and Peg G was comparable to that of mFOLFIRINOX combined with primary prophylaxis using Peg G studies (3-5) and mFOLFIRINOX-only studies (6, 7). These previous findings along with our own suggest that FOLFIRINOX combined with using Peg G might increase the incidence of anorexia and nausea compared with mFOLFIRINOX with or without Peg G. However, we must be cautious regarding the interpretation of the data obtained by our group and Terazawa et al. (2), since the numbers of patients enrolled in both studies are limited. Thus, the incidence of nausea and anorexia accompanied by mFOLFIRINOX combined with Peg G needs to be re-evaluated in future studies including a larger number of patients.

Dr. Chen et al. raised another issue regarding the incidence of bone pain accompanied by multiple Peg G injections. As they pointed out, multiple G-CSF injections often induce bone pain. Unexpectedly, we did not experience the discontinuation of mFOLFIRINOX regimen due to musculoskeletal pain in this study despite multiple injections of Peg G. The lack of patients complaining of musculoskeletal pain might be attributed to the fact that the primary disease in our study was advanced pancreatic cancer, and many patients were being administered non-steroidal anti-inflammatory drugs (NSAIDs) for cancer-related pain relief. Given that NSAIDs are effective in relieving both bone pain and cancer-related pain, it is likely that the administration of NSAIDs might have ameliorated bone pain.

Finally, Dr. Chen et al. argue that it is too early to determine the cost-effectiveness of mFOLFIRINOX combined with Peg G. We agree with this opinion and feel that large-scale, multi-center prospective trials will be required in order to determine the cost-effectiveness. Such future studies will be useful for assessing not only the cost-effectiveness but also the non-hematological toxicities of mFOLFIRINOX combined with Peg G.

The authors state that they have no Conflict of Interest (COI).

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References

1. Yamao K, Takenaka M, Yoshikawa T, et al. Clinical safety and efficacy of secondary prophylactic pegylated G-CSF in advanced pancreatic cancer patients treated with mFOLFIRINOX: a single-center retrospective study. Intern Med **58**: 1993-2002, 2019.
2. Terazawa T, Goto M, Miyamoto T, et al. Efficacy of prophylactic G-CSF in patients receiving FOLFIRINOX: a preliminary retrospective study. Intern Med **54**: 2969-2973, 2015.
3. Blazer M, Wu C, Goldberg RM, et al. Neoadjuvant modified (m) FOLFIRINOX for locally advanced unresectable (LAPC) and borderline resectable (BRPC) adenocarcinoma of the pancreas. Ann Surg Oncol **22**: 1153-1159, 2015.
4. Mahaseth H, Brutcher E, Kauh J, et al. Modified FOLFIRINOX regimen with improved safety and maintained efficacy in pancreatic adenocarcinoma. Pancreas **42**: 1311-1315, 2013.
5. Stein SM, James ES, Deng Y, et al. Final analysis of a phase II study of modified FOLFIRINOX in locally advanced and metastatic pancreatic cancer. Br J Cancer **114**: 737-743, 2016.
6. Ozaka M, Ishii H, Sato T, et al. A phase II study of modified FOLFIRINOX for chemotherapy-naive patients with metastatic pancreatic cancer. Cancer Chemother Pharmacol **81**: 1017-1023, 2018.
7. Yoshida K, Iwashita T, Uemura S, et al. A multicenter prospective phase II study of first-line modified FOLFIRINOX for unresectable advanced pancreatic cancer. Oncotarget **8**: 111346-111355, 2017.

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