

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 57030

Title: First-line chemotherapy in very elderly patients with metastatic pancreatic cancer:
Gemcitabine monotherapy versus Combination chemotherapy

Reviewer's code: 02547883

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: South Korea

Manuscript submission date: 2020-05-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-05-30 02:22

Reviewer performed review: 2020-05-31 04:16

Review time: 1 Day and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This was retrospective cohort study to compare the effectiveness of first-line chemotherapy in very elderly patients with metastatic pancreatic cancer, specially emphasis on gemcitabine monotherapy versus combination chemotherapy. Contrary to the results in the elderly group, the effect of combination chemotherapy was similar to that of gemcitabine monotherapy in the very elderly group, while the incidence of adverse event was lower in the gemcitabine treatment arm. The author concluded that gemcitabine monotherapy may be superior for choice in very elderly patients compared to treat metastatic pancreatic adenocarcinoma. The study concept, methods for analysis, statistical procedures, and description were generally considered appropriate except for several parts, as being described below with page number 1 from the title page. Page 4, lines 24; “dp” must be forgotten to delete. Correct appropriately. Page 4, lines 26; The author is required to mention why to defined elderly as 65-74 years old and very elderly as ≥ 75 years old, for example by citing domestic or international guidelines regarding to the geriatrics. Page 10, lines 2-; The first paragraph seemed to be confusing, as I think the results are interpreted in reverse. Page 12, lines 11-; Since table 4 showed the appearance of AE but not conducted in the analysis for each of the two groups as elderly vs. very elderly, it is not possible to conclude “gemcitabine monotherapy may be superior for managing metastatic pancreatic cancer in very elderly patients compared with combination therapy in terms of adverse event” based only on the dose reduction rate in whole cohort including elderly and very elderly. Furthermore, it may be necessary to show by multivariate cox regression analysis that gemcitabine monotherapy was not a poor prognostic factor in the very elderly.

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 57030

Title: First-line chemotherapy in very elderly patients with metastatic pancreatic cancer:
Gemcitabine monotherapy versus Combination chemotherapy

Reviewer's code: 00045989

Position: Peer Reviewer

Academic degree: AGAF, FACC, FACP, FASGE, MD

Professional title: Director, Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: South Korea

Manuscript submission date: 2020-05-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-05-28 00:36

Reviewer performed review: 2020-06-02 21:12

Review time: 5 Days and 20 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The manuscript by Han et al analyzes 104 patients over age 65 with pancreatic cancer, comparing those over 75 years of age with those between 65 – 74. Fifty-nine patients were treated with combination chemotherapy (gemcitabine versus gemcitabine plus nab-paclitaxel and FOLFIRINOX) and 45 with monotherapy. Primary outcomes included PFS and OS. Unsurprisingly, the baseline characteristics were significantly different between the two chemotherapy groups and two age groups. Two-thirds of those patients between 65 – 74 years old were treated with combination therapy (49/74) versus 1/3 of 30 patients in 75 years and older. In attempt to compare outcomes between the two groups, you have done propensity score matching. Unfortunately, it has led to very few patients in either group: (50 total patients 65 – 74 years, 25 Rx with monotherapy and 25 with combination Rx versus 20 patients 75 years and older, 10 in each group. This makes statistical comparisons fraught with the potential for a beta error.

1. There seems to be a significant discordance in CA 19-9 between the 65 – 74 year-old group and those ≥ 75 years. Given that biliary obstruction alone can be a cause of CA 19-9 elevation, did any of these patients have jaundice?
 - a. Had any of these patients, particularly those with a head lesion, undergone biliary bypass or endoscopic stenting?
 - b. Did any of these patients have previous pancreatic resection?
2. You mention that neutrophil-lymphocyte ratio, CA 19-9, ECOG status, and tumor burden are all associated with pancreatic cancer prognosis, yet you fail to mention that infectious complications related to neutropenia or cholangitis from an obstructed biliary prosthesis are factors associated with survival.
3. In the Discussion, you state: “We demonstrated that G mono has similar efficacy to combination chemotherapy...” Actually, your study shows the opposite. Combination therapy appears to have better outcomes in patients between 65 – 74 years and comparable outcomes in older patients, likely because of underlying health



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issues, intolerance of side effects, baseline ECOG status, and inability to infuse full doses of chemotherapy.

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 57030

Title: First-line chemotherapy in very elderly patients with metastatic pancreatic cancer:
Gemcitabine monotherapy versus Combination chemotherapy

Reviewer's code: 03878293

Position: Editorial Board

Academic degree: PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: South Korea

Manuscript submission date: 2020-05-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-05-28 23:15

Reviewer performed review: 2020-06-03 05:07

Review time: 5 Days and 5 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The manuscript entitled, "First-line chemotherapy in very elderly patients with metastatic pancreatic cancer: Gemcitabine monotherapy versus Combination chemotherapy" is interesting. The authors have retrospectively evaluated the clinical responses of gemcitabine monotherapy (i.e., G mono) and combination chemotherapy (i.e., gemcitabine plus nab-paclitaxel and FOLFIRINOX) in the elderly (i.e., 65–74 years old) and very elderly (i.e., ≥75 years old) pancreatic ductal adenocarcinoma cancer (PDAC) patients. The primary outcomes of assessing the clinical responses of these therapies were progression-free survival (PFS) and overall survival (OS). The median PFS and OS in the elderly patients were found to be longer in the combination chemotherapy group compared to very elderly patients. Consistent with the findings of other clinical studies, the adverse events were more frequently observed in the combination chemotherapy group than in the G mono group. While the combination therapy was found to be more effective than G mono in elderly patients, G mono was superior for the management of metastatic pancreatic cancer in very elderly patients. Overall, the current studies provided the rationale of exploring G mono in very elderly patients, which also strengthened the previously published data demonstrating that G mono should be used in older patients or those with low Eastern Cooperative Oncology Group (ECOG) performance status. I have a few minor comments. 1. Please use "0" before point (.) wherever applicable. For example, use $p=0.020$ instead of $p=.020$. 2. The reference style should be consistent. For example, in reference 1, the first author's name is bold.

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 57030

Title: First-line chemotherapy in very elderly patients with metastatic pancreatic cancer:
Gemcitabine monotherapy versus Combination chemotherapy

Reviewer's code: 00077340

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: South Korea

Manuscript submission date: 2020-05-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-05-28 13:17

Reviewer performed review: 2020-06-09 09:42

Review time: 11 Days and 20 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

In this submission from Sung Yong Han's group, the authors report that when the first-line chemotherapy is considered in very elderly patients with metastatic pancreatic cancer, gemcitabine monotherapy is superior for the management of metastatic pancreatic cancer in very elderly patients. This is a potentially interesting report that may affect the first-line chemotherapy in very elderly patients with metastatic pancreatic cancer. But there are some issues to be discussed more. The authors should consider the following comments. 1) The authors reported that the gemcitabine mono group in the elderly group had fewer chemotherapy cycles and a lower second-line chemotherapy transition rate compared with the combination chemotherapy group. The authors should explain why such a result occurred. 2) The authors, like other tables, should classify adverse events into the elderly group and the very elderly group and described in Table 4.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 57030

Title: First-line chemotherapy in very elderly patients with metastatic pancreatic cancer:
Gemcitabine monotherapy versus Combination chemotherapy

Reviewer's code: 00077340

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: South Korea

Manuscript submission date: 2020-05-27

Reviewer chosen by: Dong-Mei Wang (Technical Editor)

Reviewer accepted review: 2020-07-24 08:01

Reviewer performed review: 2020-07-24 10:30

Review time: 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors generally answer my questions appropriately. I have no more questions.