

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 55512

Title: Comparison of Efficacy Between Adjuvant Chemotherapy and Chemoradiation Therapy for Pancreatic Cancer After R0 Resection: AJCC Stage-based Approach

Reviewer's code: 02543905

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: South Korea

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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 Grade E: Do not publish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 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 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

First of all I congratulate authors for the effort done in retrieving data, analyzing them and drafting the manuscript. The manuscript is substantially a retrospective study performed on a single institution database and covering a long period of 13 years. The population of the study is of 355 patients that is fair enough to draft some conclusion. The paper is written in a fair language that needs a deep polishing by a native English speaker, the structure of the paper is concordant to journal guidelines, Stats are appropriated and bibliography is complete, updated and well cited. Furthermore, there are many issues that, in my opinion, need to be addressed. First of all: in the text there are references to tables and figures that are not present in the file that I was allowed to download. Major issues:

- 1) Authors should better clarify the difference between Chemoradiation (CRT) and Radiotherapy plus systemic Chemotherapy since it appears to be the same thing. By reading through the text one may argue that CRT plus SCT means that patients received CT either during RT or as maintenance treatment after the initial one. This sounds a bit confusing after all and needs to be clarified. Of course groups need to be renamed according to the treatment (I guess) as RT alone, CT alone and CRT. Furthermore, authors should clarify which were the issues that addressed the choice of giving RT 45 - 55 Gy 6 to 8 weeks or 20 Gy for 10 consecutive days repeatedly. As written in the section "mats and Meths" it sounds somewhat arbitrary.
- 2) Chemotherapies administration associated to RT should be clarified for doses and treatment scheme.
- 3) "the proportion of patients with a free margin of < 1 mm was highest in the CT alone group". Well this may be a major selection bias since it is well known that RT increases the local recurrence free survival for these patients and, in my opinion, this should be addressed in the discussion. Moreover I think that the issue "stage III local recurrence" should be considered according to the "locally advanced" instead of



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

the N2 condition. 4) comparing duration of treatment of CT and CRT with RT alone makes no sense at all. The paper appears, to me, as a bit confused and definitely lacks a structured organization of the study groups. Maybe for the missing tables, some parts are really difficult to understand at the first read. While describing the results of each treatment, I'd create some marked separation among groups and describe the results in the same groups according to either AJCC stage or disease-free margin. After that, I'd compare the results of a single group and related subgroups with Others. Minor issues: 1) in the abstract, there is no mention of the secondary endpoints. 2) Introduction is far too long and needs to be shortened and simplified. 3) Since you're dealing with cancer staging, the extent of lymphadenectomy routinely performed should be described. In conclusion, the paper deals with an open problem in oncologic surgery, it is well designed and well discussed. The number of patients is large enough to drive some conclusion with the obvious limit of the retrospective design. The major weakness of the study lies in the language limits and a big confusion in the organization of results' description. Maybe that this can be enhanced by the lack of the tables and figures, I don't know. I think that this is an overall valuable study that might be taken into proper consideration for publication after addressing the outlined issues anyway not in the present form.

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Name of journal: World Journal of Clinical Oncology

Manuscript NO: 55512

Title: Comparison of Efficacy Between Adjuvant Chemotherapy and Chemoradiation Therapy for Pancreatic Cancer After R0 Resection: AJCC Stage-based Approach

Reviewer's code: 03091510

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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 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
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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

Min Su You and coworkers present a study of a total of 335 patients who underwent resection and adjuvant treatment for pancreatic cancer. Adjuvant therapy consisted of chemoradiation therapy (CRT), systemic chemotherapy (SCT), or combined treatment of chemoradiation plus chemotherapy therapy (CRT-SCT). For stage I-II disease overall survival did not differ. For 59 patients with stage III median overall survival in SCT group (19.0 months) and CRT-SCT group (23.4] months) was significantly longer than that in CRT group (17.7 months; $P=0.011$ and $P<0.001$, respectively). The study is well performed and nicely written and presents a large, single center experience on different adjuvant therapy regimens in resected pancreatic cancer. The adjuvant SCT and/or CRT regimen was determined by multidisciplinary discussions with each patient. Since the decision to undergo CRT, SCT or CRT-SCT was undertaken in an “off-protocol” setting in the study hospital, some information about the selection criterias for the three different adjuvant regimens in the authors institution should be presented in the Methods section. Please define R0 resection. 1 mm rule? How many patients underwent R1 resection at the study centre during the study period? In the Results section it s stated that 126 (37.6%) patients had a safety margin of less than or equal to 0.1 cm=R1 according to current definitons. Thus the title of the manuscript is misleading. Isn't this paper actually describing both R0 and R1 resections? In the discussion the authors state that adjuvant treatment for pancreatic cancer is not yet standardized. mFOLFIRINOX is now the preferred adjuvant regimen in fit patients in current international guidelines from NCCN, European Society for Medical Oncology, and American Society of Clinical Oncology (ASCO). Alternatively, doublet therapy with gemcitabine and capecitabine or monotherapy with gemcitabine or 5-fluorouracil plus leucovorin can be offered. Patients given CRT-SCT in the current study were younger

and had better performance status than the other two groups. In light of the recent PRODIGE study would mFOLFIRINOX be considered as adjuvant regimen in the study hospital for these patients? ESPAC-1 (reference 22, RCT) showed that adjuvant chemotherapy had a significant survival benefit in patients with resected pancreatic cancer, whereas adjuvant chemoradiotherapy had a deleterious effect on survival when radiotherapy is given before chemotherapy. Of note, the two studies cited in favor of adjuvant CRT (reference 13 and 24) are not randomized clinical trials as ESPAC-1.