

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6854

Title: S-1 in the treatment of pancreatic cancer.

Reviewer code: 00505466

Science editor: Qi, Yuan

Date sent for review: 2013-10-30 20:30

Date reviewed: 2013-11-12 18:43

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Major revision

COMMENTS TO AUTHORS

The authors provide a comprehensive overview of the use of S-1 in pancreatic cancer. Some commenst are to be made. The major advantage of oral instead of intravenous administration of S-1 should be noted in the introduction. This is issue is only discussed in the section regarding chemoradiation. It should be transferred from there to the introduction. In the section entitled "First-line chemotherapy with S-1 for unresectable pancreatic cancer" the authors mix unresectable with metastatic pancreatic cancer. Hence, the title should be changes or data separated in two paragraphs. "GEM plus erlotinib, FOLFIRINOX or GEM plus nab-paclitaxel are accepted treatment options": 'Nab' in nab-paclitaxel should be fully written (nanoparticle albumin-bound) the first time noted with abbreviation in parentheses. Similarly, this is the case for 'FOLFIRINOX'. Furthermore, 'or' should be replaced by 'and'. The results of these schemes should be noted, so the reader can compare the results of the S1 treatments with those 'standard' treatments. What were the results of the early phase II study of reference 14? What do the authors mean with "late phase II study"? Were the GS studies in metastatic or locally advanced pancreatic cancer? Since the S-1 results were within the range of the GS studies, why is the GS combination considered favorable? The terms 'unresectable', 'locally advanced' and 'metastatic' are inconsistently used through the text. For example, the phase II study was for metastatic or locally advanced pancreatic cancer and the conclusion is that S1 is one of the options for unresectable pancreatic cancer. The authors conclude "GS therapy, as well as other GEM and fluoropyrimidine combinations, would not be accepted as the alternative to the standard chemotherapy with GEM alone" for metastatic/unresectable pancreatic cancer. While progression free survival was probably better for GS in the three randomized studies,

overall survival was better for GS in two randomized phase II studies and probably only equal in the phase III GEST study due to second line treatment with S-1 in the GEM group. Hence, it seems from these data that GS might be more beneficial than GEM alone. So please explain why this conclusion? Regarding second-line treatment, it would be interesting for the reader to provide the data from the Pelzer study to know what the survival data are for best supportive care to be able to compare those with the various second-line chemotherapy data. For second-line treatment S-1 combinations only on progression free survival data have been discussed, while in the last randomized phase II study also overall survival was improved. In the section concerning chemoradiation, "Instead of using S-1, capecitabine based CRT has been reported in Western counties", counties should be corrected in "countries". It would be interesting for the reader to provide survival data on locally advanced pancreatic cancer without treatment. Further, the issue of eventually making irresectable pancreatic cancer resectable by chemoradiation should be discussed. In the section regarding adjuvant chemotherapy, "Chemotherapy with GEM has been accepted as the standard treatment based on the results of randomized controlled studies", please add 'adjuvant'. The indication criteria for adjuvant chemotherapy should be noted (Every case? Node positive disease? Positive margins?). Please provide also a table of the randomized studies on adjuvant chemotherapy. In Future perspectives, "This clinical questions should be addressed in future studies", 'questions' should be replaced by 'question'.

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6854

Title: S-1 in the treatment of pancreatic cancer.

Reviewer code: 02544990

Science editor: Qi, Yuan

Date sent for review: 2013-10-30 20:30

Date reviewed: 2013-11-30 10:43

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)	language polishing	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

In this review, the authors present the clinical efficacy of S-1 in the treatment of pancreatic cancer. They present and review the results of current S-1 based clinical trials, especially focus on recent two studies in Japan. The compact result summary of the trials with comparison to GEM based chemotherapy is described and it is easy to read and understand the issue throughout this review. The manuscript needs some minor revisions deserving for publication in this journal. Comments (1) In regard to a section of first-line chemotherapy, the authors should express clearly whether “metastatic” or “unresectable” pancreatic cancer patients each trials involved with. “Unresectable” term includes local advanced pancreatic cancer. (2) In regard to adjuvant chemotherapy, the authors should describe more clinical and basic discussion about “surprising results” of JASPAC-01 study, because I guess this result is core of S-1 efficacy. (3) In future perspectives, the authors should cite references about current “neoadjuvant chemotherapy” or “sequential radical surgical therapy” and correlate S-1 therapy.

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6854

Title: S-1 in the treatment of pancreatic cancer.

Reviewer code: 02527475

Science editor: Qi, Yuan

Date sent for review: 2013-10-30 20:30

Date reviewed: 2014-03-09 12:51

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	language polishing	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This paper is a well written summary of the efficacy of TS-1 in the treatment of pancreatic cancer. The history of introduction of TS-1 and the rolls of TS-1 in the treatment of pancreatic cancer as the first-line regimen, the second-line regimen, and the adjuvant therapy regimen have been described briefly. In the section of adjuvant chemotherapy, the authors commented only on the results of ESPAC-01 trial in Japan. However, the roll of the other previous trials in Japan, including negative results, should have great contribution to establish the basis of clinical trials for the treatment of pancreatic cancer. In this sense, the authors should address the first positive results by JSAP-02 in this section, not only including in the Table 7. The result of JSAP-02 was very similar to that of CONOKO-01, but the first Japanese trial with improved PFS of patients with resectable pancreatic cancer.