Author’s response to reviews

Title: Efficacy and safety of weekly nab-paclitaxel plus gemcitabine in Chinese patients with metastatic adenocarcinoma of the pancreas: a phase II study

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Author’s response to reviews:
Dear Editors:

Thank you for the opportunity to revise this manuscript to address this additional reviewer’s (reviewer #3) comments. We were pleased to learn that our changes were acceptable to the previous reviewer (reviewer #2). We have made every effort to address each applicable comment from reviewer #3. Please see below for a detailed description of how each comment was addressed. Also, please note that these changes are highlighted throughout the manuscript.

Reviewer #3:

From a cancer epidemiology standpoint, this trial was well planned but reporting may be improved.

Comment 1: Since you reported survival results at two different updates, you should cite the correspondent median (range) follow-up and not only its median; the same for age in table 1.

We have added the median (range) follow-up for both survival analyses (p 10, lines 223 and 225). We have also added the range for age in Table 1.

The median OS was 9.2 months (95% CI, 7.6-11.1; Figure 1), and the 1-year OS rate was 30% (95% CI, 14%-47.6%); 15% of patients survived for ≥ 15 months. The median follow-up for OS was 8.9 months (range, 0.7-15.1 months). In an updated analysis approximately 1 year later, the median OS was 9.3 months, with a median follow-up of 14.6 months (range, 0.7-21.7 months). The 12-month OS rate was 32% in the follow-up analysis.

Comment 2: “If an insufficient number of 158 responses was observed after Stage 1 or 2, the study would progress to Part 3” normally, using Simon design, when you get a few responses, the study will be stopped; you did the opposite, please clarify why and how.

The Simon design was followed in our study. For Part 1, the criterion of > 2 responses was used to enroll an additional 54 patients into Part 2; if < 2 responses were observed, the study would have terminated at that time. In addition, the Simon design was used to stop the study from progressing into Part 3 because the predetermined number of patients responded (>9/82) in Part 2.

Comment 3: The title should reflect which part of your trial is now presented.

This report includes results from each part of the trial. Part 3 was not initiated since the prespecified independently assessed ORR endpoint for Part 2 was met.
Comment 4: RECIST 1.0, why not v. 1.1?

RECIST version 1.0 was used in this trial to be consistent with methods implemented in the global phase III trial.

Comment 5: CT 3.0, why not 4.0-1?

NCI CTCAE 3.0 was used in this trial to be consistent with methods implemented in the global phase III trial.

Comment 6: “correlation with clinical outcomes” please use potential association, not correlation (all around the manuscript).

The manuscript has been amended in the 2 locations that it previously appeared to incorporate the language of “potential association” (p 7, lines 172 and lines 176).

Exploratory endpoints were disease control rate (the percentage of patients achieving objective tumor response or stable disease for ≥ 16 weeks), serum carbohydrate antigen 19-9 levels and potential association with clinical outcomes, patient-reported quality of life using the European Organisation of Research and Treatment of Cancer Quality of Life Questionnaire-Core 30, and tumor biomarker analysis. Ad hoc analyses included progression-free survival (PFS) and potential association with baseline neutrophil-to-lymphocyte ratio (NLR) and OS. Efficacy was evaluated in the intent-to-treat population, which included all enrolled patients.

Comment 7: 0%CR + 35%PR + 22%SD + 16%PD = 73% + 28% not assessable = 101% (mind Table 2).

The percentages in Table 2 are higher than 100% due to rounding. We have included a footnote in the table to indicate this.

Comment 8: “Results from this phase II study in Chinese patients are positive” I don’t agree, see above.

Per the Simon 2-stage design, Part 2 was positive, so Part 3 was not needed.
Comment 9: “The nab-paclitaxel/gemcitabine regimen used in MPACT was efficacious” I don’t agree, see above.

Findings from the MPACT trial were positive and led to the regulatory approval of nab-paclitaxel/gemcitabine as a treatment option for patients with metastatic pancreatic cancer. The nab-paclitaxel/gemcitabine regimen used in MPACT resulted in a median OS of 8.7 months in the overall population and a median OS of 9.2 months in the current study of Chinese patients. These results in Chinese patients are indeed very promising for this patient population.

Comment 10: Table 4 is not a comparison (since no inferential test was done), it’s a mere report.

We have amended the title of Table 4 to address this point.

Comment 11: Poor figure quality, moreover figure 2 should be omitted (no play for NLR).

We have verified the figure quality with the journal. We did not omit this figure since a similar analysis was done in the MPACT study.

Best regards,

Lin Shen