



Submitted by:
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NCCN Guidelines Panel: Pancreatic Adenocarcinoma

Dear NCCN Pancreatic Adenocarcinoma Guidelines Panel:

On behalf of Celgene Corporation, we respectfully request that the NCCN Pancreatic Adenocarcinoma Guidelines Panel review recently updated data regarding the use of Abraxane[®] (albumin-bound paclitaxel) for metastatic pancreatic cancer.

Specific Changes:

We respectfully request an update to the Discussion surrounding Systemic Therapy Approaches (MS-15) for pancreatic adenocarcinoma to reflect the most recently presented results from the Phase III MPACT (Metastatic Pancreatic Adenocarcinoma Clinical Trial), including updated overall survival (OS) data. Additionally, albumin-bound paclitaxel in combination with gemcitabine is currently recommended for the treatment of metastatic pancreatic adenocarcinoma in patients with good performance status (defined as ECOG 0-1 with good pain management, patent biliary stent, and adequate nutritional intake) with a Category 1 rating. We request NCCN update this listing and recommend the use of albumin-bound paclitaxel in patients with metastatic pancreatic cancer in the “poor performance status” section as a preferred treatment option with a Category 1 rating and add language to the Guidelines section for metastatic disease and the Discussion surrounding Systemic Therapy Approaches (MS-15) for pancreatic adenocarcinoma to indicate that patients with a KPS ≥ 70 were also included in the MPACT.

FDA Clearance:

On September 6, 2013, the FDA approved albumin-bound paclitaxel for the treatment of metastatic adenocarcinoma of the pancreas as first-line treatment, in combination with gemcitabine. Please refer to the enclosed prescribing information for the FDA-approved indications as well as safety information.

Rationale for Suggested Change:

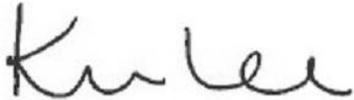
Results of a post-hoc analysis of the Phase III MPACT were recently published.¹ Overall survival (OS) was reported from an updated data cutoff as of May 9, 2013. In the intent-to-treat population, the updated median OS in the albumin-bound paclitaxel plus gemcitabine arm was 8.7 months (95% CI 7.89-9.69) compared to 6.6 months (95% CI 6.01-7.2) in the gemcitabine arm; HR=.72 (95% CI .62-.83), $P < .0001$. No new safety signals were observed for either arm at the time of this analysis.

Consistent with the results for the overall population, a significant overall survival benefit favoring albumin-bound paclitaxel plus gemcitabine compared to gemcitabine alone was observed in subgroups based on performance status (of pertinence, KPS 70-80 median overall survival 7.6 months vs. 4.3 months, respectively, HR=.59; $P < .001$). Consistent with the breadth of data considered in patients with poor performance status, there were 30 patients with a KPS score of 70 in the nab-paclitaxel plus

gemcitabine arm in the MPACT.² Additionally, albumin-bound paclitaxel plus gemcitabine at various doses and schedules was well tolerated in 24 advanced or metastatic pancreatic cancer patients that had an ECOG PS of 2.³ A KPS categorization of 60-70 can be converted to an ECOG PS of 2.⁴

Your consideration of this submission is greatly appreciated.

Sincerely,



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Victoria Manax, MD
Exec Director, US Medical Affairs Disease Lead – Pancreatic

Cited References:

1. Goldstein D, El-Maraghi RH, Hammel P, et al. nab-Paclitaxel plus gemcitabine for metastatic pancreatic cancer: long-term survival from a phase III trial. *J Natl Cancer Inst.* 2015;107(2). <http://www.ncbi.nlm.nih.gov/pubmed/25638248>.
2. Tabernero J, Chiorean EG, Infante JR, et al. Prognostic factors of survival in a randomized phase III trial (MPACT) of weekly nab-paclitaxel plus gemcitabine versus gemcitabine alone in patients with metastatic pancreatic cancer. *Oncologist.* 2015;20(2):143-50. <http://www.ncbi.nlm.nih.gov/pubmed/25582141>.
3. Guillen-Ponce C, Lopez R, Macarulla T, et al. A phase I/II trial to evaluate the efficacy and safety of nab-paclitaxel in combination with gemcitabine for the treatment of frail patients with advanced or metastatic pancreatic cancer: Safety results of the Phase I trial [Poster]. Poster presented at: 39th Congress of the European Society for Medical Oncology (ESMO); September 26–30, 2014; Madrid, Spain.
4. Ma C, Bandukwala S, Burman D, et al. Interconversion of three measures of performance status: an empirical analysis. *Eur J Cancer.* 2010;46(18):3175-83. <http://www.ncbi.nlm.nih.gov/pubmed/20674334>.