



July 12, 2010

Submission Request c/o Joan McClure
National Comprehensive Cancer Network
500 Old York Road, Suite 250
Jenkintown, PA 19046

RE: Updated Clinical Evidence in Support of Oxaliplatin in Pancreatic Cancer

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Date of request: July 12, 2010
NCCN Guidelines Panel: Pancreatic Cancer

Dear Ms. McClure,

As the NCCN Pancreatic Cancer Panel reviews emerging evidence for this cancer type, on behalf of sanofi-aventis U.S., I respectfully request consideration of the inclusion of oxaliplatin in combination with 5-fluorouracil, leucovorin, and irinotecan (FOLFIRINOX) as first-line treatment of metastatic pancreatic cancer.

Oxaliplatin in Combination with 5-fluorouracil, Leucovorin, and Irinotecan (FOLFIRINOX) as First-Line Therapy for Metastatic Pancreatic Cancer

This request is for the NCCN Pancreatic Cancer Panel to review the FOLFIRINOX data from the phase III study by Conroy et al.¹ and to consider the addition of this regimen as first-line therapy for metastatic pancreatic cancer patients.

FOLFIRINOX was compared with gemcitabine in 342 patients as first-line treatment of metastatic pancreatic cancer.¹ The primary endpoint was overall survival. A total of 250 patients were treated and evaluable for response. FOLFIRINOX demonstrated statistically significant greater overall survival (10.5 months vs 6.9 months, HR=0.61, P<0.001), progression free survival (6.4 months vs 3.4 months, P<0.0001), and response rate (27.6% vs 10.9%, P=0.0008) over treatment with gemcitabine. Grade 3/4 toxicities in FOLFIRINOX versus gemcitabine included diarrhea (12.3% vs 1.6%), nausea (15.6% vs 6.3%), vomiting (17.2% vs 6.3%), fatigue (24% vs 14.3%), neutropenia (47.9% vs 19.2%), and febrile neutropenia (5.7% vs 0). There were no toxic deaths. The authors concluded treatment with FOLFIRINOX resulted in significantly greater overall survival, progression free survival, and response rate than gemcitabine as first-line treatment of metastatic pancreatic cancer, with manageable toxicities.

Specific changes recommended within the guidelines

Please update the "Principles of Chemotherapy" (PANC-E) section to include FOLFIRINOX as a first-line treatment option for metastatic pancreatic cancer.

FDA Status

Oxaliplatin is not FDA-approved for use in patients with pancreatic cancer.

Rationale for recommended change

FOLFIRINOX is the first regimen that demonstrated significantly longer overall survival, progression free survival and response rate than gemcitabine alone.

Literature support

1. Conroy T, Desseigne F, Ychou M, et al. Randomized phase III trial comparing FOLFIRINOX (F: 5FU/leucovorin [LV], irinotecan [I], and oxaliplatin [O]) versus gemcitabine (G) as first-line treatment for metastatic pancreatic adenocarcinoma (MPA): Preplanned interim analysis results of the PRODIGE 4/ACCORD 11 trial [abstract]. *J Clin Oncol* ; 2010. 28(15S, pt 1);303s. Abs 4010.
2. Conroy T, Desseigne F, Ychou M, et al. Randomized phase III trial comparing FOLFIRINOX (F: 5FU/leucovorin [LV], irinotecan [I], and oxaliplatin [O]) versus gemcitabine (G) as first-line treatment for metastatic pancreatic adenocarcinoma (MPA): Preplanned interim analysis results of the PRODIGE 4/ACCORD 11 trial [abstract]. Presented at the 46th Annual Meeting of the American Society of Clinical Oncology, Chicago, Illinois, USA, June 4-8, 2010. Abs4010. Available at: http://www.asco.org/ASCOv2/MultiMedia/Virtual+Meeting?&vmview=vm_session_presentations_view&confID=74&sessionID=340. Accessed July12, 2010.

We appreciate the opportunity to provide this information for consideration by the NCCN Pancreatic Cancer Panel. If you have any questions or require additional information, please do not hesitate to contact me at (908) 981-7287 or via e-mail at julia.petses@sanofi-aventis.com. Thank you for your time and consideration.

Sincerely,

Julia Petses, PharmD
Director, Oncology/Urology Medical Information Services
sanofi-aventis U.S.

Enclosures: Copies of referenced primary literature