



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 Docetaxel 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 docetaxel in combination with gemcitabine and capecitabine (GTx) as first-line treatment for metastatic pancreatic cancer.

**Docetaxel in Combination with Gemcitabine and Capecitabine as First-Line Therapy for Metastatic Pancreatic Cancer**

This request is for the NCCN Pancreatic Cancer Panel to review Fine et al.<sup>1-3</sup> and to consider the addition of docetaxel in combination with gemcitabine and capecitabine (GTx) as first-line therapy for advanced and metastatic pancreatic cancer patients. Previous to 2009, overall survival had not yet been reached; overall and 1-and 2-year survival data was presented at the 2009 American Society of Clinical Oncology Annual Meeting.<sup>1</sup>

The GTx treatment regimen was evaluated as first-line therapy in 43 patients with metastatic pancreatic cancer.<sup>1</sup> The primary endpoint was response rate, determined by RECIST criteria. A total of 41 patients were evaluable by intent to treat analysis. Nine (21.9%) and 17 (41.5%) had a partial response and stable disease, respectively. The median overall survival was 14.5 months and median time to treatment failure was 6.9 months. One and 2-year survival rates were 56% and 14.6%, respectively. Grade 3/4 toxicities included leucopenia (31.6%), neutropenia (29.2%), thrombocytopenia (12.2%), infection (12.5%), and mucositis (7.5%). The authors concluded that GTx demonstrated activity and greater than 1-year survival in patients with metastatic pancreatic cancer.

Additionally, GTx was evaluated 44 patients with advanced pancreatic cancer.<sup>2,3</sup> A partial response was achieved in 47% and disease stabilization in 28% of 32 patients with metastatic disease. A partial response was achieved in 47% and stable disease in 28% of 32 patients with metastatic disease. Among 12 patients who presented with inoperable disease, radiation therapy followed chemotherapy and then Whipple procedure; 67% achieved a complete response (successful Whipple with normal CA 19-9 levels) and 25% achieved a partial response. Grade 3 toxicities included leucopenia (25%), asthenia (20%), diarrhea (20%), and erythrodysesthesia (15%). The authors concluded that the triplet regimen of docetaxel/capecitabine/gemcitabine was efficacious and well tolerated in the treatment of pancreatic cancer.

**Specific changes recommended within the guidelines**

Please update the "Principles of Chemotherapy" (PANC-E) section to add GTx as a first-line treatment option in patients with metastatic pancreatic cancer.

**FDA Status**

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

**Rationale for recommended change**

The GTx regimen demonstrated overall survival greater than 1 year and may be a treatment option as first-line therapy for metastatic pancreatic cancer.

**Literature support**

1. Fine RL, Moorer G, Sherman W, et al. Phase II trial of GTx chemotherapy in metastatic pancreatic cancer. *J Clin Oncol*. 2009;27(15S, pt 1):232s. Abs 4623.
2. Fine RL, Fogelman DR, Sherman W, et al. The GTx regimen: a biochemically synergistic combination for advanced pancreatic cancer (PC) [abstract]. *Proc Am Soc Clin Oncol*. 2003; 22:281. Abstract 1129.
3. Fine RL, Sherman W, Fogelman D, et al. The GTx regimen: biochemically synergistic chemotherapy for advanced pancreatic cancer [poster]. Presented at 39th Annual Meeting of the American Society of Clinical Oncology, Chicago, IL, USA, May 31-June 3, 2003. Poster 1129.

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