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# A Near-Complete Response to Treatment with Gemcitabine plus *nab*<sup>®</sup>-Paclitaxel in a Patient with Metastatic Pancreatic Cancer and Poor Performance Status: A Case Report

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## Key Words

Gemcitabine · Metastatic · *nab*<sup>®</sup>-Paclitaxel · Pancreatic cancer · Poor performance status

## Abstract

Patients with metastatic pancreatic adenocarcinoma and poor performance status (PS) are typically excluded from clinical trials of new systemic treatments. Due to concerns that such patients cannot tolerate the greater toxicity sometimes associated with combination chemotherapy regimens, the recommended treatment for pancreatic cancer patients with poor PS is gemcitabine monotherapy. We report the case of a 79-year-old female with pancreatic adenocarcinoma metastatic to the lungs, with multiple comorbidities and an Eastern Cooperative Oncology Group PS of 3, who achieved a rapid and prolonged objective response to gemcitabine plus *nab*<sup>®</sup>-paclitaxel. The patient received a total of 11 cycles of treatment. Although her disease was well controlled with gemcitabine plus *nab*-paclitaxel, she died just over 11 months after diagnosis as a result of her comorbid conditions compounded by treatment-related hematologic toxicity. This case suggests that patients with metastatic pancreatic adenocarcinoma and poor PS may benefit from first-line combination therapy with gemcitabine plus *nab*-paclitaxel. Further study of this regimen in such patients is warranted.

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## Introduction

Pancreatic cancer is the fourth most common cause of cancer-related death in the US [1]. It is predicted that, in 2014, pancreatic cancer will account for approximately 7% (more than 39,500 cases) of all cancer deaths in the US, with more than 46,000 new cases being anticipated [1]. Prognosis is particularly poor, with a 5-year survival of 6%, falling to 2% in those diagnosed with distant disease [1].

Gemcitabine monotherapy has been the standard treatment for advanced pancreatic cancer since 1997, after clinical trials demonstrated symptomatic benefits with gemcitabine, including alleviation of pain and improved performance status (PS), as well as modest improvements in overall survival (OS) [2, 3]. More recently, phase III trials have demonstrated that, compared with gemcitabine monotherapy, treatment with gemcitabine in combination with the epidermal growth factor receptor inhibitor erlotinib [4], *nab*<sup>®</sup>-paclitaxel [5], or FOLFIRINOX (oxaliplatin, irinotecan, fluorouracil, and leucovorin) [6] significantly increases OS in patients with metastatic pancreatic adenocarcinoma, with manageable toxicity. However, these trials excluded patients with poor PS. Eligibility criteria for the trial of gemcitabine plus erlotinib included an Eastern Cooperative Oncology Group (ECOG) PS of 0, 1, or 2 [4]; in the trial of gemcitabine plus *nab*-paclitaxel [the Metastatic Pancreatic Adenocarcinoma Clinical Trial (MPACT)], a Karnofsky PS of at least 70 was required for inclusion [5] (70 on the Karnofsky PS scale correlates to an ECOG PS of 2 [7]); and eligibility for inclusion in the gemcitabine plus FOLFIRINOX trial required an ECOG PS of either 0 or 1 [6].

The National Comprehensive Cancer Network (NCCN) currently recommends combination chemotherapy for patients with pancreatic adenocarcinoma and good PS (ECOG 0 or 1), but advocates gemcitabine monotherapy with best supportive care for those with poor PS [8]. Further research is required to establish optimal management strategies for pancreatic adenocarcinoma patients with poor PS.

This paper reports the case of a patient with poor PS who achieved a prolonged objective response to combination therapy with gemcitabine plus *nab*-paclitaxel. The patient gave informed consent for the publication of details of her case, as she wanted future pancreatic cancer patients to benefit from her experience.

## Case Report

A 79-year-old Caucasian female with metastatic pancreatic cancer and poor PS (ECOG 3) was referred to the author's clinic on May 6, 2013. The patient had a history of hypothyroidism, hyperlipidemia, hypertension, gastroesophageal reflux disease, Parkinson's disease, supranuclear ophthalmoplegia, and torticollis. Her medication included aspirin, mometasone furoate, metoprolol, verapamil, omeprazole, rosuvastatin, levothyroxine, and carbidopa-levodopa. The patient was wheelchair bound because of her Parkinson's disease.

An abdominal computed tomography (CT) scan on May 3, 2013 revealed a pancreatic head mass of 3.1 cm, with obstruction of the bile, pancreatic, and common bile ducts. Retroperitoneal peripancreatic mesenteric adenopathy and abnormal appearance of the colon suggested colonic or pancreatic malignancy. The scan also showed metastases in the lung, where nodules of up to 1.5 cm in diameter were observed. A biopsy of the pancreas on May 6 confirmed adenocarcinoma of intermediate to high grade, most likely of pancreatic origin.

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At the initial consultation with the author, the patient was informed of her advanced disease and advised to enter a hospice because of her poor PS. However, the patient rejected this advice, stating that she wanted to ‘fight’ her cancer. Further investigations were therefore initiated, with the aim of administering palliative chemotherapy.

On May 10, 2013, a plastic stent was inserted by endoscopic retrograde cholangiopancreatography at the Springfield Memorial Hospital, Springfield, Ill., USA. A positron emission tomography (PET) CT scan on May 17 confirmed the results of the previous scan and showed abnormal uptake in the pancreatic head, with a standardized uptake value of 11.5 (fig. 1a). Further uptake in the left lower nodule and the appearance of small, noncalcified nodules suggested metastatic disease. The mesenteric lymph nodes were slightly enlarged. At this time, the carbohydrate antigen (CA) 19-9 level was elevated at 7,925 IU/ml (normal value 0–34 IU/ml).

The patient was referred for chemotherapy and started treatment with gemcitabine plus *nab*-paclitaxel on May 20, 17 days after the first CT scan. Gemcitabine was administered at the standard dose of 1,000 mg/m<sup>2</sup>. However, because of the patient’s age, the dose of *nab*-paclitaxel was arbitrarily decreased from 125 mg/m<sup>2</sup>, which is the approved dose for administration in combination with gemcitabine, to 100 mg/m<sup>2</sup>. Both agents were administered on days 1, 8, and 15 of a 28-day cycle.

On June 27, 2013, a permanent metallic stent was placed in the patient’s common bile duct at the Springfield Memorial Hospital. During the third cycle of gemcitabine plus *nab*-paclitaxel, a PET CT scan revealed a near-complete response of the metastatic pancreatic cancer (fig. 1b); CA 19-9 had fallen to 374 IU/ml. As had been explained to the patient at the outset, the goal of therapy had been to stabilize her disease while hoping for a tumor response. The magnitude of the response and the preservation of the patient’s quality of life that resulted were quite unexpected.

The fifth treatment cycle was interrupted because the patient was experiencing tremors, probably due to progression of her Parkinson’s disease (no other cause was identified). Investigations revealed a low hemoglobin (Hb) level (8.8 g/dl). This was considered to be treatment related, and was supported with transfusions. A drop in PS further delayed the chemotherapy, but cycle 5 was restarted after a 1-month delay.

A PET CT scan during cycle 6 showed a continued response compared with the initial scan, but also a slight increase in tumor size compared with the scan during cycle 3, possibly due to tumor growth during the 1-month delay in dosing. A further PET CT scan at the start of cycle 9 (after 8 months of treatment) suggested improved disease and no increase in activity within the head of the pancreas, as had been seen in the previous scan. A small pleural effusion of the left lung and borderline hypermetabolic disease were observed, thought to be secondary to early pneumonia. The patient’s CA 19-9 level remained relatively low, at approximately 420–480 IU/ml.

During the course of treatment, the patient received additional blood and platelet transfusions in response to low Hb levels on three occasions (Hb decreased from 12.5 g/dl at baseline to 8.8 g/dl on September 8, 2013 and January 6, 2014, and to 9.2 g/dl on March 12, 2014), and in response to thrombocytopenia also on three occasions (platelet counts of 46,000, 47,000, and 28,000/μl on April 2, 5, and 7, 2014, respectively). Two episodes of neutropenia occurred during the first few months of treatment – absolute neutrophil counts of 440 and 380 cells/mm<sup>3</sup> were recorded on June 12 and August 26, 2013, respectively – but did not recur subsequently, and there was no evidence of peripheral neuropathy after 11 cycles of gemcitabine plus *nab*-paclitaxel. The patient was admitted to hospital on April 3, 2014 with pulmonary edema and wheezing. A CT scan revealed bilateral pleural effusions; these were considered to be secondary to the multiple transfusions that she had received.

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She also had episodes of aspiration of pneumonia, and continued to decline functionally. Although her cancer was well controlled (CA 19-9 was 393 IU/ml on March 19, 2014), the patient's comorbid conditions, in addition to poor tolerance of the chemotherapy, led to her death on April 14, 2014.

## Discussion

In recent years, several combination chemotherapy regimens have shown efficacy superior to that of single-agent chemotherapy (typically gemcitabine) in patients with advanced metastatic pancreatic cancer [4–6, 9, 10]. Despite efficacy benefits, combination regimens have traditionally been associated with higher rates of toxicity. For example, in the PRODIGE 4/ACCORD 11 trial, FOLFIRINOX significantly and dramatically improved median OS (11.1 vs. 6.8 months), as well as progression-free survival and objective response rate, compared with gemcitabine monotherapy [6]. However, the combination regimen was associated with significantly higher rates of grade 3–4 toxicities, including neutropenia, febrile neutropenia, thrombocytopenia, diarrhea, and sensory neuropathy [6]. Notably, this trial included only relatively robust patients; those aged >75 years or with ECOG PS ≥2 were excluded. In addition, two recent meta-analyses comparing gemcitabine-based combination therapy with gemcitabine monotherapy concluded that, while the combination regimens significantly improve OS, treatment-related toxicity is increased [9, 10]. Consequently, current NCCN guidelines continue to recommend gemcitabine monotherapy for patients with metastatic pancreatic cancer and poor PS, who may be unable to tolerate the greater toxicity of combination regimens [8]. It should be noted, however, that combination therapies are not always associated with increased toxicity compared with single-agent gemcitabine. For example, the combination of gemcitabine plus erlotinib has been reported to lead to a small but significant improvement in OS without substantially impacting on toxicity [4].

Concerns about the potential impact of treatment-related toxicity on quality of life are understandable, even when the survival benefit is considerable (as with FOLFIRINOX), given that rates and severities of toxicity differ markedly between treatments. However, data from the PRODIGE 4/ACCORD 11 trial showed that FOLFIRINOX maintains or improves quality of life (based on the measurement of overall global health status) to a greater extent than gemcitabine monotherapy [11]. Using data from the phase 3 MPACT, which compared gemcitabine 1,000 mg/m<sup>2</sup> plus *nab*-paclitaxel 125 mg/m<sup>2</sup> with gemcitabine 1,000 mg/m<sup>2</sup> alone [5], quality-adjusted time without symptoms or toxicities (Q-TWiST) analyses found that treatment with gemcitabine plus *nab*-paclitaxel led to a significant and clinically important 21% improvement in quality-adjusted survival (Q-TWiST) compared with gemcitabine monotherapy in treatment-naïve patients with metastatic pancreatic adenocarcinoma [12]. Other case reports have suggested that gemcitabine plus *nab*-paclitaxel is an effective and well-tolerated option in patients with pancreatic cancer – albeit those with good PS – in clinical practice. Three reports relate to patients with metastatic disease who had failed prior chemotherapy (two after FOLFIRINOX, one after failure of two different gemcitabine-based regimens) [13–15]; another describes a patient with locally advanced pancreatic cancer who was treated with gemcitabine plus *nab*-paclitaxel in a neoadjuvant setting [16].

The favorable efficacy findings and acceptable toxicity observed in MPACT and in case studies suggest that there may be a place for gemcitabine plus *nab*-paclitaxel in the treatment of patients with pancreatic cancer and poor PS. However, as patients with a Karnofsky PS of <70 (approximately equivalent to ECOG PS >2) were excluded from MPACT,

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supporting data are lacking. The present report describes the case of a patient with advanced metastatic pancreatic cancer and poor PS (ECOG 3) at presentation. The patient showed a remarkable, near-complete response after only 2 months of chemotherapy with gemcitabine plus *nab*-paclitaxel. Further improvement was noted after 8 months of treatment. At the time of her death (just over 11 months after diagnosis, due to her comorbid conditions compounded by poor tolerance of the hematologic toxicity of treatment), the patient's tumor was well controlled; moreover, she had survived for longer than the median OS of patients with good PS in MPACT (8.5 months).

To the author's knowledge, this is the first published report of a patient with metastatic pancreatic adenocarcinoma and an ECOG PS of only 3 demonstrating a near-complete response to treatment with gemcitabine plus *nab*-paclitaxel. The current recommended treatment for such patients is gemcitabine monotherapy; however, the case described here suggests that this population could benefit from first-line combination therapy with gemcitabine plus *nab*-paclitaxel. These findings suggest that further study of first-line gemcitabine plus *nab*-paclitaxel in pancreatic cancer patients with poor PS is warranted in a clinical trial setting.

### Acknowledgements

Sanjeev Silwal, a medical student from the Universal College of Medical Sciences, Tribhuvan University, Nepal, and Dr. Prajwal Dhakal of the Institute of Medicine, Maharajgunj Campus, Kathmandu, Nepal, assisted with collecting data and obtaining PET scan images. Medical writing support was provided by Jo Chapman and Sandralee Lewis of the Investigator Initiated Research Writing Group (part of KnowledgePoint 360 Group, an Ashfield Company), and was funded by Celgene.

### Disclosure Statement

The author receives honoraria as a speaker for Celgene.

### References

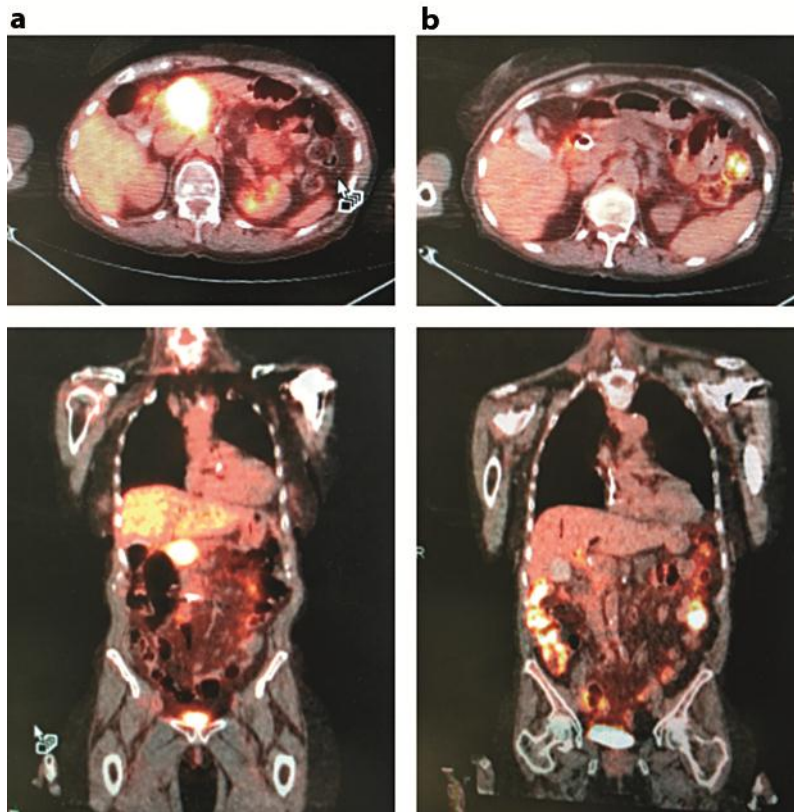
- 1 American Cancer Society: Cancer Facts & Figures. 2014. <http://www.cancer.org/research/cancerfactsstatistics/cancerfactsfigures2014/index> (accessed June 2, 2014).
- 2 Carmichael J, Fink U, Russell RC, Spittle MF, Harris AL, Spiessi G, Blatter J: Phase II study of gemcitabine in patients with advanced pancreatic cancer. *Br J Cancer* 1996;73:101–105.
- 3 Burris HA 3rd, Moore MJ, Andersen J, Green MR, Rothenberg ML, Modiano MR, Cripps MC, Portenoy RK, Storniolo AM, Tarassoff P, Nelson R, Dorr FA, Stephens CD, Von Hoff DD: Improvements in survival and clinical benefit with gemcitabine as first-line therapy for patients with advanced pancreas cancer: a randomized trial. *J Clin Oncol* 1997;15:2403–2413.
- 4 Moore MJ, Goldstein D, Hamm J, Figer A, Hecht JR, Gallinger S, Au HJ, Murawa P, Walde D, Wolff RA, Campos D, Lim R, Ding K, Clark G, Voskoglou-Nomikos T, Ptasynski M, Parulekar W; National Cancer Institute of Canada Clinical Trials Group: Erlotinib plus gemcitabine compared with gemcitabine alone in patients with advanced pancreatic cancer: a phase III trial of the National Cancer Institute of Canada Clinical Trials Group. *J Clin Oncol* 2007;25:1960–1966.
- 5 Von Hoff DD, Ervin T, Arena FP, Chiorean EG, Infante J, Moore M, Seay T, Tjulandin SA, Ma WW, Saleh MN, Harris M, Reni M, Dowden S, Laheru D, Bahary N, Ramanathan RK, Tabernero J, Hidalgo M, Goldstein D, Van Cutsem E, Wei X, Iglesias J, Renschler MF: Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. *N Engl J Med* 2013;369:1691–1703.
- 6 Conroy T, Desseigne F, Ychou M, Bouché O, Guimbaud R, Bécouarn Y, Adenis A, Raoul JL, Gourgou-Bourgade S, de la Fouchardière C, Bannoun J, Bachet JB, Khemissa-Akouz F, Péré-Vergé D, Delbaldo C, Assenat E,

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- Chauffert B, Michel P, Montoto-Grillot C, Ducreux M; Groupe Tumeurs Digestives of Unicancer; PRODIGE Intergroup: FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. *N Engl J Med* 2011;364:1817–1825.
- 7 Buccheri G, Ferrigno D, Tamburini M: Karnofsky and ECOG performance status scoring in lung cancer: a prospective, longitudinal study of 536 patients from a single institution. *Eur J Cancer* 1996;32A:1135–1141.
  - 8 National Comprehensive Cancer Network (NCCN) Clinical Practice Guideline in Oncology: Pancreatic Adenocarcinoma. Version 2. 2014. [http://www.nccn.org/professionals/physician\\_gls/pdf/pancreatic.pdf](http://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf) (accessed June 3, 2014).
  - 9 Sun C, Ansari D, Andersson R, Wu DQ: Does gemcitabine-based combination therapy improve the prognosis of unresectable pancreatic cancer? *World J Gastroenterol* 2012;18:4944–4958.
  - 10 Ciliberto D, Botta C, Correale P, Rossi M, Caraglia M, Tassone P, Tagliaferri P: Role of gemcitabine-based combination therapy in the management of advanced pancreatic cancer: a meta-analysis of randomised trials. *Eur J Cancer* 2013;49:593–603.
  - 11 Gourgou-Bourgade S, Bascoul-Mollevi C, Desseigne F, Ychou M, Bouché O, Guimbaud R, Bécouarn Y, Adenis A, Raoul JL, Boige V, Bérille J, Conroy T: Impact of FOLFIRINOX compared with gemcitabine on quality of life in patients with metastatic pancreatic cancer: results from the PRODIGE 4/ACCORD 11 randomized trial. *J Clin Oncol* 2013;31:23–29.
  - 12 Reni M, Wan Y, Solem C, Whiting S, Ji X, Botteman M: Quality-adjusted survival with combination nab-paclitaxel + gemcitabine vs gemcitabine alone in metastatic pancreatic cancer: a Q-TWiST analysis. *J Med Econ* 2014;17:338–346.
  - 13 Berger AK, Weber TF, Jäger D, Springfield C: Successful treatment with nab-paclitaxel and gemcitabine after FOLFIRINOX failure in a patient with metastasized pancreatic adenocarcinoma. *Onkologie* 2013;36:763–765.
  - 14 Klimant E, Markman M, Albu DM: Clinically meaningful responses to sequential gemcitabine-based chemotherapy regimens in a patient with metastatic pancreatic cancer. *Case Rep Oncol* 2013;6:72–77.
  - 15 Portal A, Pernot S, Siauve N, Landi B, Lepère C, Colussi O, Rougier P, Zaanani A, Verrière B, Taieb J: Sustained response with gemcitabine plus nab-paclitaxel after folfirinnox failure in metastatic pancreatic cancer: report of an effective new strategy. *Clin Res Hepatol Gastroenterol* 2014;38:e23–e26.
  - 16 Olowokure O, Torregroza-Sanchez MP, Bedoya-Apaez ID: Gemcitabine plus nab-paclitaxel with chemoradiation in locally advanced pancreatic cancer (LAPC). *J Gastrointest Oncol* 2013;4:E16–E18.



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**Fig. 1.** PET scans prior to treatment (a) and after 2 months of gemcitabine plus *nab*-paclitaxel chemotherapy (b).