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ORIGINAL RESEARCH

# Performance status dynamics during treatment with *nab*-paclitaxel plus gemcitabine versus gemcitabine alone for metastatic pancreatic cancer

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**Objectives:** This analysis examined changes in Karnofsky performance status (KPS) as a surrogate for patient's well-being during treatment with *nab*-paclitaxel plus gemcitabine vs gemcitabine alone as first-line therapy for metastatic pancreatic cancer (MPC) in the Phase III MPACT trial.

**Participants and methods:** Descriptive analyses were performed for KPS at three time points (3 and 6 months after randomization and 1 month before disease progression) and for time to any KPS deterioration. Time to definitive KPS deterioration (≥10-point KPS decrease from baseline) was calculated using the Kaplan–Meier method. A larger decrease from baseline (≥20 points) was investigated as a sensitivity analysis. A Cox proportional hazards model analyzed the effect of baseline factors (including treatment) potentially associated with time to definitive deterioration.

**Results:** The two treatment arms had generally comparable time to any KPS deterioration, similar KPS at 3 and 6 months after randomization and at 1 month before disease progression, and no significant difference in time to definitive deterioration. Baseline KPS, neutrophil-to-lymphocyte ratio, age, liver metastases, and region had a significant effect on time to definitive KPS deterioration, but treatment arm did not.

**Conclusion:** The increased survival observed with *nab*-paclitaxel plus gemcitabine was not associated with adverse effects on performance status.

**Keywords:** Karnofsky performance status, metastatic pancreatic cancer, chemotherapy, *nab*-paclitaxel, gemcitabine

## Introduction

More than one-half of pancreatic cancer diagnoses are made when the disease has already reached the metastatic stage.[1] The survival statistics associated with metastatic pancreatic cancer (MPC) are dismal: the 5-year survival rate in the USA is just 2.7%.[1] The psychological impact of such a diagnosis, along with the prevalence of severe symptoms and treatment-related toxicities, may affect a patient's quality of life (QoL).[2,3] The importance of maintaining QoL is highlighted by a study surveying patients diagnosed with pancreatic cancer and pancreatic cancer caregivers in which QoL was the second most important concern after extending life.[3] As treatments in MPC continue to increase survival, it becomes more important to monitor a patient's

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ability to engage in everyday activities to ensure that the gains in survival do not negatively affect QoL.

The standard of care for the first-line treatment of MPC is chemotherapy, which can stabilize health-related QoL and improve pain control.[4,5] The Karnofsky performance status (KPS) scale assesses patient ability to carry on normal activity, perform work, live at home, and care for personal needs and is graded in 10-point decrements ranging from 100 (no evidence of disease or symptoms) to 0 (death).[6] Therefore, assessing changes in KPS during treatment may be a reasonable surrogate for the impact of treatment on patient's well-being.

The Phase III MPACT trial, which enrolled patients with MPC and KPS values ≥70, demonstrated superior efficacy of *nab*-paclitaxel plus gemcitabine vs gemcitabine alone for all endpoints, including overall survival (median, 8.7 vs 6.6 months; hazard ratio [HR] 0.72 [95% confidence interval {CI}: 0.62, 0.83]; $P<0.001$) and progression-free survival (median, 5.5 vs 3.7 months; HR 0.69 [95% CI: 0.58, 0.82]; $P<0.001$).[7,8] The favorable results from this large international trial have led to *nab*-paclitaxel plus gemcitabine being a standard first-line treatment for patients with MPC and good performance status.[5] QoL data in MPACT were not prospectively collected; however, a subsequent analysis found that treatment with *nab*-paclitaxel plus gemcitabine was associated with significantly greater quality-adjusted time without symptoms or toxicities (Q-TWiST) than gemcitabine alone.[9]

The objective of this analysis was to examine changes in KPS during first-line treatment with *nab*-paclitaxel plus gemcitabine vs gemcitabine alone for patients with MPC in the MPACT study. KPS was intended to represent a surrogate for patient's well-being, and assessments were conducted in the overall population, as well as in patient subsets.

# Participants and methods

## Study design and participants

The MPACT study design and patient characteristics have been described previously.[8] Briefly, patients with MPC and KPS values ≥70 were enrolled. Patients experiencing a ≥10% decrease in KPS between baseline and 72 hours before randomization were excluded. Patients received either *nab*-paclitaxel 125 mg/m$^2$ followed by gemcitabine 1000 mg/m$^2$ weekly for 3 weeks followed by 1 week of rest or gemcitabine 1000 mg/m$^2$ alone weekly for the first 7 of 8 weeks and then weekly for 3 weeks followed by 1 week of rest. Randomization was stratified by the presence of liver metastases, geographic region, and baseline KPS (70–80 vs 90–100). Treatment continued until disease progression or unacceptable toxicity. The primary endpoint of the trial was overall survival. Independent ethics committees at each participating institution approved the trial, which was conducted in accordance with the International Conference on Harmonisation E6 requirements for Good Clinical Practice.[8] All patients provided written informed consent before initiating the study.

## KPS measurement

KPS was measured at baseline, 72 hours before randomization, weekly during treatment, at the end of study, and during adverse event (AE) resolution.

## Statistical analysis

### Descriptive analyses of KPS

Median KPS score for the overall group and each treatment arm was calculated at 3 and 6 months after randomization and 1 month before disease progression. Time to any KPS deterioration was evaluated in patient subgroups defined by baseline KPS score (70–80 and 90–100) and age (≥65 and <65 years).

### Time to KPS deterioration

Time to KPS deterioration was evaluated in the following two ways: 1) time to any deterioration and 2) time to definitive deterioration. The time to any deterioration was calculated using descriptive statistics and defined as the time interval between the randomization date and the date of the last visit before first KPS score deterioration (ie, maximum time to maintain baseline KPS). The time to definitive deterioration was analyzed by the Kaplan–Meier method (arms compared by log-rank test) and defined as the interval between randomization and the first time at which KPS score dropped ≥10 points from baseline. For the time to definitive deterioration analysis, censoring was applied in patients who had no KPS score reduction from baseline (at the time of last follow-up) or who had a ≥10-point reduction in KPS from baseline with a secondary improvement. The KPS for patients who died was not imputed; patients were followed up until the last available KPS assessment. Time to definitive deterioration was analyzed in the overall population, as well as in patient subsets defined by baseline age, KPS score, and neutrophil-to-lymphocyte ratio (NLR).

For the assessment of sensitivity of the time to definitive deterioration approach, a larger decrease was also investigated (KPS decrease ≥20 points).

### Multivariate modeling of time to definitive deterioration

A Cox proportional hazards model was used to estimate the relationship between the following variables and time until definitive KPS deterioration: treatment arm (*nab*-paclitaxel plus gemcitabine vs gemcitabine alone); baseline KPS score (70–80 vs 90–100); age (<65 vs ≥65 years); sex (female vs male); baseline NLR (≤5 or not recorded vs >5); geographic region (Western Europe, Eastern Europe, and Australia vs North America); pancreatic tumor location (head vs other locations [body, tail, and unknown]); presence of biliary stent; previous Whipple procedure; presence of liver, lung, or peritoneum metastases; stage at diagnosis (IV vs others); number of metastatic sites (2, 3, or ≥4 vs 1); and baseline carbohydrate antigen 19-9 level (upper limit of normal [ULN] <59 × ULN, ≥59 × ULN, and not recorded vs normal).

# Results

## Patients

Baseline characteristics for the MPACT trial have been previously reported.[8] In this analysis, KPS assessments at baseline and ≥1 postbaseline time point were available for 858 patients randomized to receive *nab*-paclitaxel plus gemcitabine (n=429) or gemcitabine alone (n=429). All relevant ethical approvals from institutional review boards/independent ethics committees were obtained prior to study commencement (refer Supplementary materials for details). Written informed consent was obtained from all patients prior to study entry.

## Descriptive analysis of time to KPS deterioration

In the overall population, the time to any deterioration in KPS (by descriptive statistics) was ~1 month in both the *nab*-paclitaxel plus gemcitabine and the gemcitabine alone groups (median duration, 29.0 days in both groups; Table 1). The two treatment arms demonstrated the following median times to any KPS deterioration in the specified subgroups: patients with baseline KPS score 70–80 (median duration, 42.0 vs 26.0 days, respectively), baseline KPS score 90–100 (median duration, 21.0 vs 30.0 days), age <65 years (median duration, 37.0 vs 28.0 days), and age ≥65 years (median duration, 21.0 vs 30.0 days).

## Descriptive analysis of KPS at 3 and 6 months after randomization and 1 month before disease progression

### Overall population

The median KPS score at baseline was 90 in both treatment arms (Figure 1). More KPS-evaluable patients remained on treatment in the *nab*-paclitaxel plus gemcitabine vs the gemcitabine alone arm at 3 months after randomization (275 [64%] vs 204 [48%] patients) and 6 months after randomization (139 [32%] vs 70 [16%] patients). The *nab*-paclitaxel plus gemcitabine and gemcitabine alone treatment arms demonstrated generally stable median KPS scores relative to baseline at all three time points, 3 months after randomization (80 vs 90, respectively), 6 months after randomization (90 for both), and 1 month before disease progression (80 for both).

### Subgroups based on baseline performance status and age

The two treatment arms had largely similar KPS scores at the three time points analyzed in subgroups based on age and KPS score. The median KPS score at 3 months after randomization for the *nab*-paclitaxel plus gemcitabine vs gemcitabine alone arm was the same in the following subgroups: patients aged <65 years (median KPS score, 90 in both) and patients with a baseline KPS score of 70–80 (median KPS score, 80 in both) or 90–100 (median KPS score, 90 in both). In patients aged ≥65 years, the median KPS score at 3 months after randomization was 80 with *nab*-paclitaxel plus gemcitabine vs 90 with gemcitabine alone.

**Table 1** Time to any KPS deterioration by descriptive statistics

| | Parameter | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Overall population | | Baseline KPS of 70–80 | | Baseline KPS of 90–100 | | Age <65 years | | Age ≥65 years | |
| | *nab*-P + Gem | Gem | *nab*-P + Gem | Gem | *nab*-P + Gem | Gem | *nab*-P + Gem | Gem | *nab*-P + Gem | Gem |
| N | 429 | 429 | 179 | 161 | 248 | 268 | 252 | 241 | 177 | 188 |
| Median, days | 29 | 29 | 42 | 26 | 21 | 30 | 37 | 28 | 21 | 30 |
| Range | 1–423 | 1–554 | 1–423 | 1–337 | 1–414 | 1–554 | 1–423 | 1–554 | 1–299 | 1–394 |
| Quartile 1–3 | 8–99 | 8–77 | 10–134 | 8–72 | 8–77 | 7–85 | 8–108 | 8–85 | 8–58 | 7–68 |

**Abbreviations:** Gem, gemcitabine; KPS, Karnofsky performance status; *nab*-P, *nab*-paclitaxel.

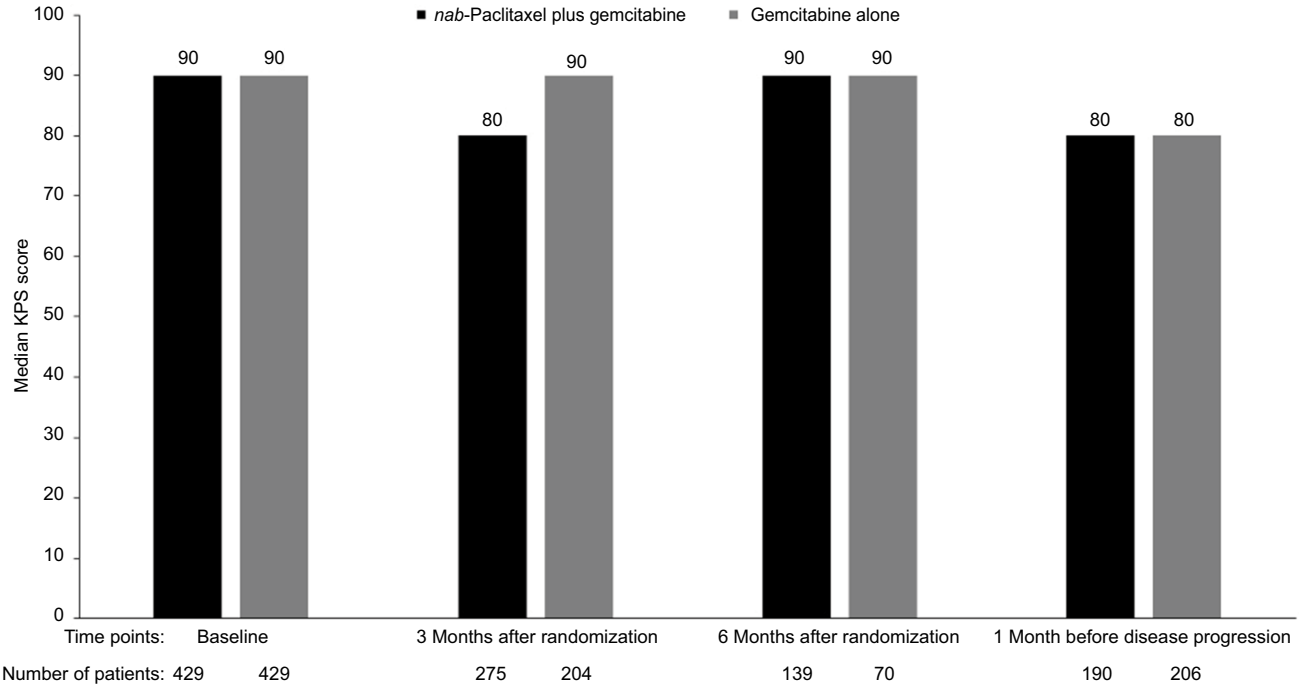


**Figure 1** Median KPS at 3 and 6 months after randomization and 1 month before progression (all patients).
**Abbreviation:** KPS, Karnofsky performance status.

The median KPS score in the following patient subgroups 6 months after randomization was the same as those 3 months after randomization for the *nab*-paclitaxel plus gemcitabine vs gemcitabine alone arms: age <65 years (median KPS score, 90 in both), age ≥65 years (median KPS score, 80 vs 90, respectively), and baseline KPS score 70–80 (median KPS score, 80 in both) or 90–100 (median KPS score, 90 in both). The median KPS score at 1 month before disease progression for the two treatment arms was the same in patients aged ≥65 years (median KPS score, 80 in both) and with baseline KPS score 70–80 (median KPS score, 80 in both) or 90–100 (median KPS score, 90 in both). In patients aged <65 years, the median KPS score 1 month before disease progression was 90 for *nab*-paclitaxel plus gemcitabine vs 80 for gemcitabine alone.

## Time to definitive KPS deterioration by Kaplan–Meier method

For the overall group, there was no statistically significant difference in the time to definitive KPS deterioration (≥10 points) in patients treated with *nab*-paclitaxel plus gemcitabine vs gemcitabine alone (median, 76 vs 74 days, respectively; HR 0.97 [95% CI: 0.81, 1.16]; *P*=0.77; Figure 2). The *nab*-paclitaxel plus gemcitabine and gemcitabine alone treatment arms were not statistically significantly different in time to definitive KPS deterioration for older (age ≥65 years; median, 44 vs 59 days, respectively; HR 1.12 [95% CI: 0.86, 1.47]; *P*=0.39) or younger (age <65 years; median, 102 vs 86 days; HR 0.90 [95% CI: 0.71, 1.14]; *P*=0.37) patients or for patients with lower baseline NLR (≤5; median, 96 vs 100 days; HR 1.04 [95% CI: 0.84, 1.30]; *P*=0.71) or higher baseline NLR (>5; median, 51 vs 41 days; HR 0.83 [95% CI: 0.61, 1.12]; *P*=0.23). Similarly, there was no statistically significant difference in time to definitive KPS deterioration observed between the *nab*-paclitaxel plus gemcitabine and gemcitabine alone arms in patients with baseline KPS values 70–80 (median, 184 vs 119 days, respectively; HR 0.78 [95% CI: 0.57, 1.08]; *P*=0.13) or 90–100 (median, 37 vs 58 days, respectively; HR 1.14 [95% CI: 0.92, 1.41]; *P*=0.23). The sensitivity analysis (time to KPS score decrease ≥20 points) confirmed that the time to definitive KPS deterioration was not statistically significantly different for *nab*-paclitaxel plus gemcitabine vs gemcitabine alone (median, 213 vs 211 days, respectively; HR 1.05 [95% CI: 0.84, 1.31]; *P*=0.70; Figure 3).

## Multivariate modeling of time until definitive deterioration

Multivariate modeling results, shown in Table 2**,** revealed that when confounding factors were controlled, treatment arm (*nab*-paclitaxel plus gemcitabine vs gemcitabine alone) was not associated with estimated time to definitive KPS deterioration (HR 1.03 [95% CI: 0.86, 1.24]; *P*=0.72). A

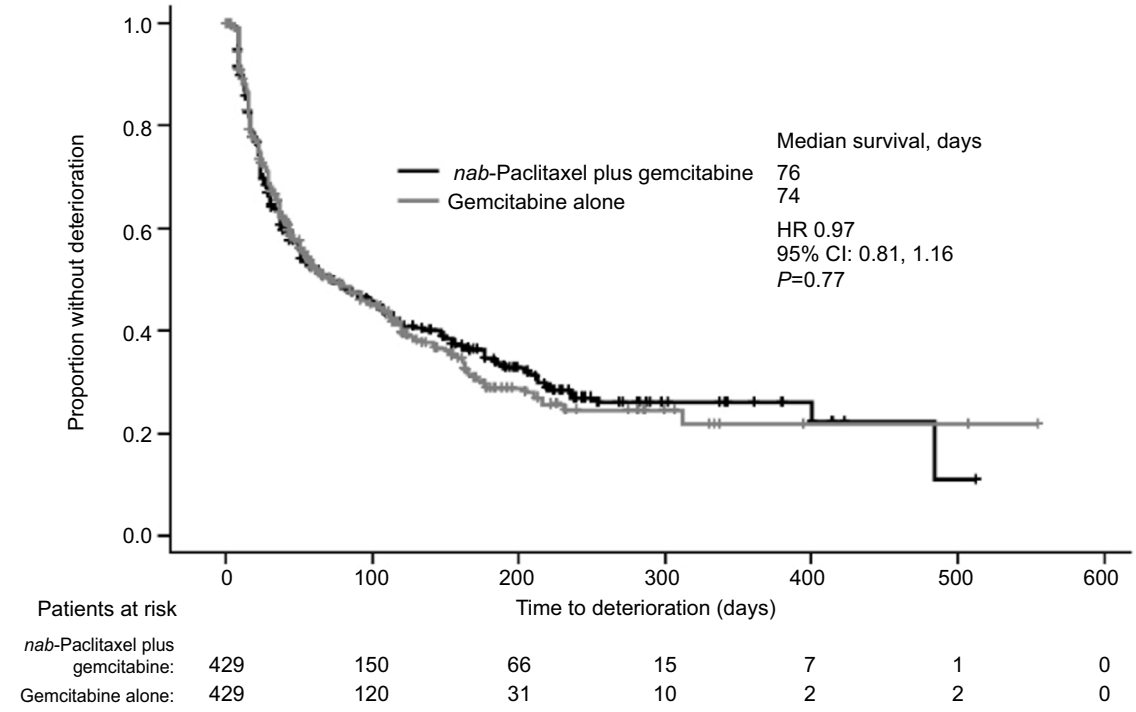


**Figure 2** Time to definitive KPS deterioration (≥10 points) by Kaplan–Meier analysis (all patients).
**Abbreviations:** CI, confidence interval; HR, hazard ratio; KPS, Karnofsky performance status.

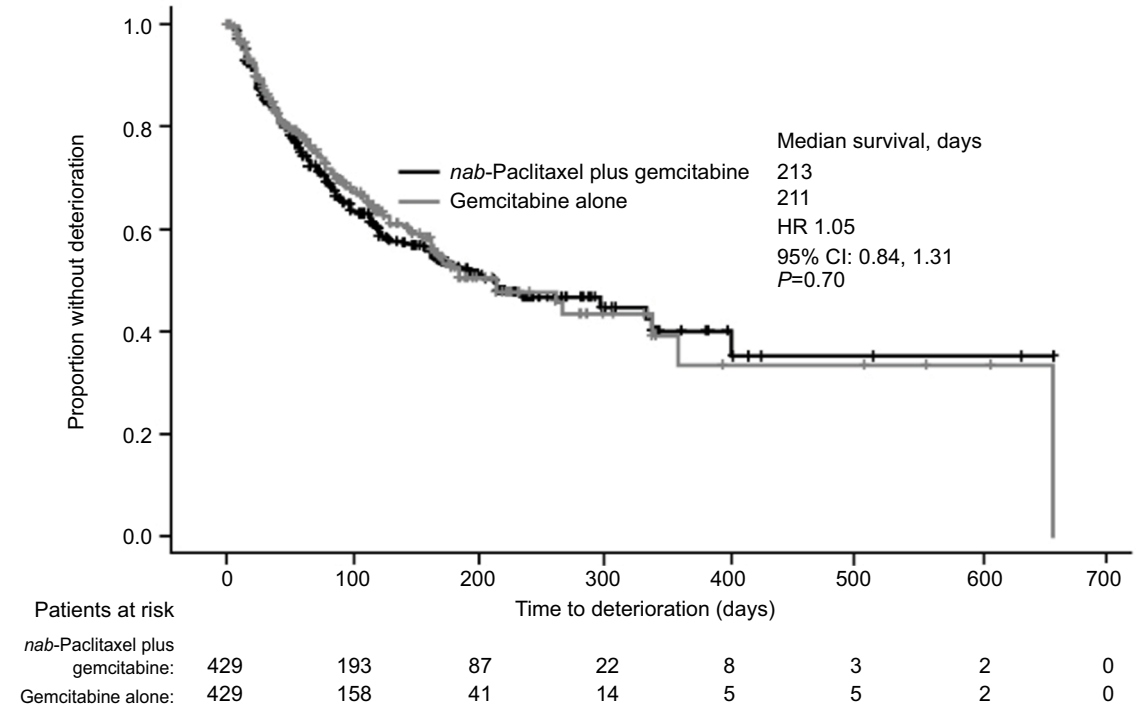


**Figure 3** Sensitivity analysis of time to definitive KPS deterioration (≥20 points; all patients).
**Abbreviations:** CI, confidence interval; HR, hazard ratio; KPS, Karnofsky performance status.

**Table 2** Proportional hazard model TUDD with patient baseline characteristics

| Variable | HR (95% CI) | *P*-value |
|---|---|---|
| ABI-007 + gemcitabine (ref = gemcitabine) | 1.03 (0.86, 1.24) | 0.721 |
| Baseline KPS 70–80 (ref = baseline KPS 90–100) | 0.52 (0.42, 0.63) | <0.0001 |
| Age <65 years (ref = age ≥65 years) | 0.82 (0.69, 0.99) | 0.040 |
| NLR | | |
| NLR ≤5 (ref = NLR >5) | 0.73 (0.60, 0.89) | 0.002 |
| Not recorded (ref = NLR >5) | 2.16 (0.92, 5.06) | 0.078 |
| Tumor located in head (ref = other locations: body, tail, and unknown) | 0.99 (0.80, 1.24) | 0.951 |
| Liver metastases present (ref = no presence) | 1.41 (1.05, 1.90) | 0.025 |
| Lung metastases (ref = no presence) | 1.13 (0.87, 1.49) | 0.360 |
| Peritoneum metastases | 1.06 (0.60, 1.87) | 0.840 |
| Number of metastatic sites (ref = one site) | | |
| Two sites | 1.13 (0.72, 1.79) | 0.594 |
| Three sites | 1.05 (0.63, 1.77) | 0.841 |
| Four or more sites | 1.08 (0.60, 1.95) | 0.797 |
| Previous Whipple procedure (ref = no procedure) | 1.13 (0.72, 1.76) | 0.605 |
| Previous biliary stent (ref = no stent) | 1.24 (0.94, 1.64) | 0.134 |
| CA 19-9 level (ref = normal) | | |
| ≥59× ULN | 1.18 (0.89, 1.56) | 0.243 |
| ULN to <59× ULN | 1.01 (0.75, 1.36) | 0.958 |
| Not recorded | 1.16 (0.79, 1.71) | 0.459 |
| Female (ref = male) | 0.95 (0.79, 1.14) | 0.551 |
| Stage IV at diagnosis (ref = other stages) | 1.16 (0.88, 1.53) | 0.306 |
| Region (ref = North America) | | |
| Australia | 0.92 (0.71, 1.20) | 0.538 |
| Eastern Europe | 0.77 (0.58, 1.03) | 0.073 |
| Western Europe | 0.58 (0.40, 0.83) | 0.003 |

**Abbreviations:** CA, carbohydrate antigen; CI, confidence interval; HR, hazard ratio; KPS, Karnofsky performance status; ref, reference; NLR, neutrophil-to-lymphocyte ratio; ULN, upper limit of normal; TUDD, time until definitive deterioration.

significantly longer time until definitive deterioration of KPS score was demonstrated for patients with lower (70–80) vs higher (90–100) baseline KPS score (HR 0.52 [95% CI: 0.42, 0.63]; $P<0.01$), lower (≤5) vs higher (>5) NLR (HR 0.73 [95% CI: 0.60, 0.89]; $P<0.01$), presence vs absence of liver metastases was associated with a significantly shorter time until definitive deterioration of KPS score (HR 1.41 [95% CI: 1.05, 1.90]; $P=0.03$), age (<65 vs ≥65 years; HR 0.82 [95% CI: 0.69, 0.99]; $P=0.04$), and the region of Western Europe vs North America (HR 0.58 [95% CI: 0.40, 0.83]; $P<0.01$).

## Discussion

This retrospective analysis of the Phase III MPACT trial revealed that KPS was maintained throughout therapy with *nab*-paclitaxel plus gemcitabine as seen 3 and 6 months after randomization and 1 month before disease progression. The *nab*-paclitaxel plus gemcitabine arm compared with the gemcitabine alone arm had a higher number of patients still receiving treatment and a largely similar median KPS score at 3 months after randomization. Furthermore, at 6 months after randomization, there were approximately twice as many patients in the *nab*-paclitaxel plus gemcitabine vs gemcitabine alone arm still on treatment with an equivalent median KPS score, which suggests increased effectiveness and comparable KPS maintenance. The time to KPS deterioration for the overall population was similar between treatment arms as assessed by descriptive analysis (time to any deterioration) and Kaplan–Meier analysis (time to definitive KPS deterioration). Multivariate modeling revealed that when other factors associated with MPC prognosis were controlled, *nab*-paclitaxel plus gemcitabine vs gemcitabine alone was not associated with significantly different times to KPS deterioration. These results highlight that the enhanced survival conferred with the addition of *nab*-paclitaxel to gemcitabine[7] did not come at the expense of a clinically meaningful reduction in KPS.

While most prognostic variables were found to be associated with lower HR in the Cox model, such as lower age, lower NLR, absence of liver metastases, and Western Europe region, patients with lower baseline KPS (70–80) had a lower hazard for time to definitive deterioration compared with those with higher baseline KPS (90–100), and this was particularly evident in the *nab*-paclitaxel plus gemcitabine arm. One hypothesis is that patients with lower baseline KPS may have derived greater clinical benefit from the chemotherapy/combination therapy, given that tumor control had a larger impact on their overall performance status and, thus, a longer time to definitive deterioration. By undergoing chemotherapy/combination chemotherapy, patients with an already high baseline KPS (90–100) may have been more likely to observe a deterioration in KPS, due to inherent toxicity from chemotherapy.

The results of this analysis are in accordance with a previous Q-TWiST analysis of the MPACT trial.[9] The Q-TWiST metric captures quality-adjusted time by dividing health states into the following: the time before disease progression without toxicity (grade ≥3), time with AEs (grade ≥3), and the time after disease progression. The previous Q-TWiST analysis demonstrated that patients treated with *nab*-paclitaxel plus gemcitabine vs gemcitabine alone experienced a significantly greater Q-TWiST score (+1.7 months [95% CI: 0.8, 2.7 months]; $P<0.05$), which the authors concluded a statistically significant and clinically meaningful gain in quality-adjusted survival. In agreement, this analysis indicated that treatment with *nab*-paclitaxel plus gemcitabine did not result in significant decreases in patient performance status from baseline or relative to treatment with gemcitabine alone.

While patient-reported outcomes offer better assessment of QoL, given the global reach and patient diversity across different countries, a limitation of the MPACT study was that it did not prospectively collect this information with established metrics. Therefore, the KPS scale, which conveys information related to patient's ability to perform tasks associated with daily life, such as the capacity to work, live at home, and care for oneself, was used to assess patient functioning and serve as a surrogate related to QoL. It should be noted that a systematic review concluded that the association between functional performance status and QoL was moderate.[10] With its inherent limitations, we used prospectively collected KPS data as a surrogate marker for QoL. The maintenance of patient well-being is critical in MPC particularly because many patients are older at the time of diagnosis.[1] Many elderly patients with MPC may present with lower functional status; for these patients, it is important for clinicians to consider the importance of prolonging survival and reducing pain without causing meaningful reductions in QoL. A systematic review supported the use of chemotherapy to stabilize health-related QoL in patients with pancreatic cancer,[4] despite the AEs associated with some agents.

In the MPACT trial, the addition of *nab*-paclitaxel to gemcitabine was associated with longer survival, along with a higher incidence of certain AEs, such as neutropenia, fatigue, and peripheral neuropathy.[8] Previous analyses of the MPACT study revealed that AEs were effectively managed with dose modifications, which may have allowed patients to remain on *nab*-paclitaxel plus gemcitabine treatment longer than gemcitabine alone (median, 3.9 vs 2.8 months, respectively).[8,11] This longer duration of treatment was associated with increased survival in patients with MPC.[12] The findings from this KPS analysis further support treatment with *nab*-paclitaxel plus gemcitabine until disease progression by demonstrating a relative maintenance of performance status up to 1 month before disease progression. Treatment with *nab*-paclitaxel plus gemcitabine until disease progression, including dose modifications if necessary, has been shown to extend patient's survival without significantly interfering with patient's well-being, despite increased toxicity vs gemcitabine monotherapy,[11] and possibly offering the option for second-line therapy for an increased number of patients.[13]

## Conclusion

The present analysis revealed similar KPS dynamics between MPACT treatment arms and demonstrated that patients' performance status was maintained with the *nab*-paclitaxel plus gemcitabine regimen. The finding that KPS was generally maintained throughout treatment across a wide range of patients reinforces the broad utility of this regimen, which in previous analyses[7,8] has demonstrated superior efficacy over gemcitabine alone for the first-line treatment of patients with MPC.

## Data availability

Data supporting this analysis are available from Celgene Corporation upon reasonable request.

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## Disclosure

EGC has received research funding from and participated in an advisory board for Celgene Corporation. DVH has served as a consultant or advisor for and received honoraria from Celgene Corporation and received research funding from HonorHealth. YW was an employee of Pharmerit International, which received research funding from Celgene Corporation. SM-D is an employee of Celgene Corporation. MB is an employee and shareholder of Pharmerit International, which received research funding from Celgene Corporation. DG has received research funding from Celgene Corporation and Pfizer and served as a consultant or advisor (unremunerated) for Celgene Corporation and Pfizer. The authors report no other conflicts of interest in this work.

## References

1. [webpage on the Internet]. *SEER Stat Facts Sheets: Pancreas Cancer*. 2017. Available from: http://seer.cancer.gov/statfacts/html/pancreas.html. Accessed April 17, 2018.
2. Clark KL, Loscalzo M, Trask PC, Zabora J, Philip EJ. Psychological distress in patients with pancreatic cancer – an understudied group. *Psychooncology*. 2010;19(12):1313–1320.
3. Engebretson A, Matrisian L, Thompson C. Pancreatic cancer: patient and caregiver perceptions on diagnosis, psychological impact, and importance of support. *Pancreatology*. 2015;15(6):701–707.
4. Kristensen A, Vagnildhaug OM, Grønberg BH, Kaasa S, Laird B, Solheim TS. Does chemotherapy improve health-related quality of life in advanced pancreatic cancer? A systematic review. *Crit Rev Oncol Hematol*. 2016;99:286–298.

5. National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology. Pancreatic Adenocarcinoma, V3*. 2017. Available from: https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed April 17, 2018.
6. Peus D, Newcomb N, Hofer S. Appraisal of the Karnofsky Performance Status and proposal of a simple algorithmic system for its evaluation. *BMC Med Inform Decis Mak*. 2013;13(1):72.
7. 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).
8. Von Hoff DD, Ervin T, Arena FP, et al. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. *N Engl J Med*. 2013;369(18):1691–1703.
9. 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(5):338–346.
10. Atkinson TM, Andreotti CF, Roberts KE, Saracino RM, Hernandez M, Basch E. The level of association between functional performance status measures and patient-reported outcomes in cancer patients: a systematic review. *Support Care Cancer*. 2015;23(12):3645–3652.
11. Scheithauer W, Ramanathan RK, Moore M, et al. Dose modification and efficacy of *nab*-paclitaxel plus gemcitabine vs gemcitabine for patients with metastatic pancreatic cancer: phase III MPACT trial. *J Gastrointest Oncol*. 2016;7(3):469–478.
12. Vogel A, Römmler-Zehrer J, Li JS, McGovern D, Romano A, Stahl M. Efficacy and safety profile of nab-paclitaxel plus gemcitabine in patients with metastatic pancreatic cancer treated to disease progression: a subanalysis from a phase 3 trial (MPACT). *BMC Cancer*. 2016;16(1):817.
13. Chiorean EG, Von Hoff DD, Tabernero J, et al. Second-line therapy after *nab*-paclitaxel plus gemcitabine or after gemcitabine for patients with metastatic pancreatic cancer. *Br J Cancer*. 2016;115(9):e13.