Weekly nab-Paclitaxel in Combination With Carboplatin Versus Solvent-Based Paclitaxel Plus Carboplatin as First-Line Therapy in Patients With Advanced Non–Small-Cell Lung Cancer: Final Results of a Phase III Trial


ABSTRACT

Purpose
This phase III trial compared the efficacy and safety of albumin-bound paclitaxel (nab-paclitaxel) plus carboplatin with solvent-based paclitaxel (sb-paclitaxel) plus carboplatin in advanced non–small-cell lung cancer (NSCLC).

Patients and Methods
In all, 1,052 untreated patients with stage IIIB to IV NSCLC were randomly assigned 1:1 to receive nab-paclitaxel weekly and carboplatin at area under the concentration-time curve (AUC) 6 once every 3 weeks (nab-PC) or 200 mg/m² sb-paclitaxel plus carboplatin AUC 6 once every 3 weeks (sb-PC). The primary end point was objective overall response rate (ORR).

Results
On the basis of independent assessment, nab-PC demonstrated a significantly higher ORR than sb-PC (33% v 25%; response rate ratio, 1.313; 95% CI, 1.082 to 1.593; \(P = .005\)) and in patients with squamous histology (41% v 24%; response rate ratio, 1.680; 95% CI, 1.271 to 2.221; \(P < .001\)). nab-PC was as effective as sb-PC in patients with nonsquamous histology (ORR, 26% v 25%; \(P = .808\)). There was an approximately 10% improvement in progression-free survival (median, 6.3 v 5.8 months; hazard ratio [HR], 0.902; 95% CI, 0.767 to 1.060; \(P = .214\)) and overall survival (OS; median, 12.1 v 11.2 months; HR, 0.922; 95% CI, 0.797 to 1.066; \(P = .271\)) in the nab-PC arm versus the sb-PC arm, respectively. Patients ≥ 70 years old and those enrolled in North America showed a significantly increased OS with nab-PC versus sb-PC. Significantly less grade ≥ 3 neuropathy, neutropenia, arthralgia, and myalgia occurred in the nab-PC arm, and less thrombocytopenia and anemia occurred in the sb-PC arm.

Conclusion
The administration of nab-PC as first-line therapy in patients with advanced NSCLC was efficacious and resulted in a significantly improved ORR versus sb-PC, achieving the primary end point. nab-PC produced less neuropathy than sb-PC.

J Clin Oncol 30. © 2012 by American Society of Clinical Oncology

INTRODUCTION

Non–small-cell lung cancer (NSCLC) is the leading cause of cancer death, with only 1% 5-year survival for stage IV NSCLC.\(^1,2\) The current standard of care in advanced NSCLC is a platinum agent combined with a third-generation therapeutic, most commonly taxanes, gemcitabine, vinorelbine, or pemetrexed.\(^1,3\) However, therapy with platinum-based doublets has reached a therapeutic plateau. In a large randomized study (N = 1,155) comparing four platinum-based regimens, none of them offered a significant clinical advantage over the others, with an overall response rate (ORR) of 19% and a median overall survival (OS) of 7.9 months for all patients.\(^4\) Similarly, a phase III study in patients with advanced NSCLC treated with cisplatin plus pemetrexed showed no improvement in tumor response rate and survival over cisplatin plus gemcitabine for all histologies; however, an improvement in survival was noted in the nonsquamous histology subset with a decrement in the squamous histology subset.\(^5,6\) In general, solvent-based paclitaxel (sb-paclitaxel) plus carboplatin, the most commonly
used taxane-platinum combination in the United States, produced 15% to 32% ORR, with 7.9 to 10.6 months of median OS. The addition of bevacizumab to sb-PC for patients with nonsquamous histology provided improved efficacy (ORR, 35%; OS, 12.3 months), albeit with an increased number of treatment-related deaths; thus, the unmet medical need for the squamous histology subsets remains.

The 130-nm albumin-bound formulation of paclitaxel (nab-paclitaxel [Abraxane]; Celgene, Summit, NJ) is a promising new agent for all histologies of NSCLC. Preclinical models suggest that nab-paclitaxel may reach the tumor microenvironment more efficiently than sb-paclitaxel via caveolea-mediated transcytosis and may be preferentially taken up by cancer cells. In clinical studies, nab-paclitaxel was safe and increased ORR and time to progression in metastatic breast cancer compared with sb-paclitaxel, and it has shown activity in various other advanced solid tumors, including melanoma, pancreatic cancer, and NSCLC. In particular, in a dose-finding study in patients with advanced NSCLC, weekly 100 mg/m² nab-paclitaxel plus every-3-weeks carboplatin at area under the curve (AUC) 6

Therapy ongoing (n = 514; 99%)

Therapy discontinued (n = 521; 100%)

Reason for discontinuation

Progressive disease (n = 275; 54%)

Unacceptable toxicities (n = 61; 12%)

Adverse events (n = 20; 4%)

Investigator discretion (n = 86; 17%)

Patient discretion (n = 65; 13%)

Protocol deviation (n = 3; < 1%)

Lost to follow-up (n = 1; < 1%)

Other (n = 0)

Censoring for progression-free survival

Patients with a PFS event (n = 297; 57%)

Patients censored (n = 224; 43%)

Reason for censoring

Completed follow-up (n = 0)

Lost to follow-up (n = 10; 2%)

PD per investigator (n = 144; 28%)

New therapy (n = 40; 8%)

≥ 2 missing response (n = 15; 3%)

Assessments followed by PFS event (n = 15; 3%)

PFS follow-up ongoing (n = 15; 3%)

Censoring for overall survival

Patients with death (n = 360; 69%)

Patients censored (n = 161; 31%)

Reason for censoring

Completed follow-up (n = 68; 13%)

Lost to follow-up (n = 26; 5%)

Follow-up ongoing (n = 67; 13%)

Patients with death (n = 384, 72%)

Patients censored (n = 147, 28%)

Reason for censoring

Completed follow-up (n = 64, 12%)

Lost to follow-up (n = 27, 5%)

Follow-up ongoing (n = 56, 11%)

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Fig 1. CONSORT diagram. nab-paclitaxel, 130-nm albumin-bound paclitaxel; PD, progressive disease; PFS, progression-free survival; sb-paclitaxel, solvent-based paclitaxel.
produced the most optimal safety and efficacy profile among the various weekly and every-3-weeks regimens, with 48% ORR and median survival more than 11 months, and was selected for this trial. On the basis of the promising results of the dose-finding study, this phase III trial compared the efficacy and safety of weekly nab-paclitaxel plus carboplatin every 3 weeks with sb-paclitaxel plus carboplatin every 3 weeks in advanced NSCLC.

This study was approved by the independent ethics committees of the participating medical institutions in Australia, Canada, Japan, Russia, Ukraine, and the United States and was conducted in accordance with the World Medical Association Declaration of Helsinki and Good Clinical Practice Guidelines of the International Conference on Harmonization. Written informed consent was obtained from all patients before study initiation.

Patients
Eligible adults had histologically/ cytologically confirmed unresectable stage IIIB (with or without pleural effusion) or stage IV NSCLC measurable by Response Evaluation Criteria in Solid Tumor (RECIST), an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1, and a life expectancy of more than 12 weeks; they were previously untreated for metastatic disease and had no radiotherapy within 4 weeks of enrollment. Prior adjuvant chemotherapy was permitted if completed 12 months before study enrollment. Patients were excluded from the study if they had untreated or symptomatic brain metastasis or if they had greater than grade 1 neuropathy (per National Cancer Institute Common Terminology Criteria for Adverse Events [NCI-CTCAE] v3.0) or a history of allergy or hypersensitivity to the study drugs.

Study Design
This multicenter, 1:1 randomized, phase III study evaluated the safety and efficacy of 100 mg/m² 30-minute infusion of nab-paclitaxel on days 1, 8, and 15 followed by carboplatin AUC 6 mg/mL/min (per Calvert formula) on day 1 every 3 weeks (nab-PC) compared with 200 mg/m² 3-hour infusion of sb-paclitaxel plus carboplatin at AUC 6 (sb-PC), both given every 3 weeks, as first-line therapy in patients with advanced NSCLC (CONSORT diagram; Fig 1). Randomization was stratified by disease stage (IIIB vs IV), age (<70 vs ≥70 years), sex (male vs female), histology (squamous vs adenocarcinoma vs others), and geographic region (North America vs Russia/Ukraine vs Japan vs Australia). Treatment of at least six cycles was encouraged but could continue in the absence of progressive disease and unacceptable toxicity per the investigator’s discretion.

Assessment of Efficacy and Safety End Points
The primary efficacy end point was ORR, which was confirmed complete response (CR) and/or partial response (PR) rate, based on blinded, centralized, independent radiologic analysis, which was agreed on with the US Food and Drug Administration (FDA) to support approval of a Section 505(b)(2) application. Spiral computed tomography scans were performed and evaluated per RECIST every 6 weeks from screening until progressive disease. The key secondary efficacy end points were progression-free survival (PFS) and OS. Survival was followed for 18 months post-treatment. Other efficacy end points were investigator-determined ORR and stable disease at ≥16 weeks. Efficacy parameters were also analyzed by strata. The safety end points were the incidence of treatment-related adverse events (TRAEs), collected weekly in each arm and graded according to NCI-CTCAE v3.0 and laboratory abnormalities.

Statistical Methods
All randomly assigned patients were evaluated for efficacy (intent-to-treat [ITT] population). As observed in a phase III study in metastatic breast cancer, it was assumed that nab-PC would have a 40% improvement in response rate versus sb-PC in advanced NSCLC. On the basis of this assumption, 1,050 patients provided 80% power to test the superiority of nab-PC over sb-PC. For the response rate, interim analysis α = .001 and final analysis α = .049, 20,21

PFS and OS were analyzed by using Kaplan-Meier methods. The planned final analyses of PFS and OS was when at least 70% of patients had an event, which provided 85% power to detect superiority of a hazard ratio (HR) of 0.80. In addition, a noninferiority analysis of PFS and OS was conducted on the basis of the European Medical Agency methodologic considerations with a 15% margin (upper bound of the HR 95% CI < -1.176).

All patients who received at least one dose of study drug (treated population) were evaluated for safety. Descriptive statistics were used to summarize the change from baseline to each visit on the Functional Assessment of Cancer Therapy-Taxane (FACT-Taxane) scale, assessed on day 1 of each cycle. Treatment arm differences in TRAEs and the FACT-Taxane scale were evaluated by using Fisher’s exact test and/or the Cochran-Mantel-Haenszel test.

Table 1. Baseline Patient Demographic and Clinical Characteristics

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<td>Smoked and still smokes</td>
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Abbreviations: ECOG, Eastern Cooperative Oncology Group; nab-PC, 130-nm albumin-bound paclitaxel + carboplatin; sb-PC, solvent-based paclitaxel + carboplatin. *Few missing values.
RESULTS

Patients

A total of 1,052 patients were randomly assigned between November 2007 and August 2009, 521 to nab-PC and 531 to sb-PC. Patient baseline characteristics were well balanced between treatment arms (Table 1). The median age was 60 years, and 85% of patients were younger than age 70 years. Patients were predominately male (75%), white (81%), smokers (73%), and had stage IV disease (79%). Patients from North America were older (median age, 65 years; 33% ≥ 70 years) than patients from Russia/Ukraine (median age, 58 years; 9% ≥ 70 years); however, they were well balanced between the arms. There were more men (79% v 65%), current smokers (51% v 26%), and patients with squamous cell histology (52% v 35%) in Russia/Ukraine than in North America, respectively.

At the time of the data cutoff for the final analyses, all but three patients had discontinued therapy. The common reasons for discontinuation were progressive disease (52%), investigator’s discretion (13%), and unacceptable toxicity without progressive disease (12%), and patient discretion (13%). Only 3% of patients received prior chemotherapy (Table 1).

Efficacy Results

On the basis of independent radiology assessment of ORR, nab-PC demonstrated a significantly higher ORR than sb-PC (33% v 25%; response rate ratio, 1.313; 95% CI, 1.082 to 1.593; P = .005; Table 2). Specifically, 170 patients (33%) in the nab-PC arm had a PR (18%), unacceptable toxicity without progressive disease (12%), and patient discretion (13%). Only 3% of patients received prior chemotherapy (Table 1).

Response Rates for the Intent-to-Treat Population and Histologic Subset Based on Independent Radiologic Assessment

<table>
<thead>
<tr>
<th></th>
<th>nab-PC</th>
<th>sb-PC</th>
<th>Response Rate Ratio*</th>
<th>95% CI</th>
<th>P†</th>
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</thead>
<tbody>
<tr>
<td>Overall response</td>
<td>n = 521</td>
<td>n = 531</td>
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<tr>
<td>Complete response</td>
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<td>21.2 to 28.6</td>
<td>1.313</td>
<td>.005</td>
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<td>Partial response</td>
<td>0</td>
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<tr>
<td>Stable disease</td>
<td>170</td>
<td>131</td>
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<tr>
<td>Progressive disease</td>
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<td>84</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Squamous subset</td>
<td>n = 229</td>
<td>n = 221</td>
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<tr>
<td>Overall response</td>
<td>94</td>
<td>54</td>
<td>18.8 to 30.1</td>
<td>1.680</td>
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<td>Nonsquamous subset</td>
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<tr>
<td>Overall response</td>
<td>76</td>
<td>78</td>
<td>20.3 to 30.0</td>
<td>1.034</td>
<td>.808</td>
</tr>
</tbody>
</table>

NOTE: The Hommel procedure was used to adjust for the three comparisons related to tumor response (overall populations and two histology subgroups). The treatment and histology interaction was based on logistic regression. Abbreviations: nab-PC, 130-nm albumin-bound paclitaxel + carboplatin; sb-PC, solvent-based paclitaxel + carboplatin. *95% CIs for response rate ratios are calculated according to the asymptotic 95% CI of the relative risk of nab-PC to sb-PC. †P-values are based on the χ² test. Stable disease was defined as ≥ 16 weeks.

Response per Histology

Independent radiology assessment revealed a significant improvement of ORR for nab-PC versus sb-PC in patients with squamous cell histology (41% v 24%; response rate ratio, 1.680; 95% CI, 1.271 to 2.221; P < .001), although nab-PC was as effective as sb-PC in patients with nonsquamous histology (26% v 25%; response rate ratio, 1.034; 95% CI, 0.788 to 1.358; P = .808; Table 2). Patients with adenocarcinoma had 26% ORR in the nab-PC arm versus 27% ORR in the sb-PC arm (P = .814). Patients with large-cell carcinoma had 33% versus 15% ORR, and patients with undifferentiated histology had 24% versus 15% in the nab-PC versus sb-PC arms, but these differences were not statistically significant.

Progression-Free Survival

There was an approximately 10% increase in PFS in the nab-PC versus sb-PC arm (HR, 0.902; 95% CI, 0.767 to 1.060; P = .214; Fig 2A). Median PFS was 6.3 months (95% CI, 5.6 to 7.0 months) in the nab-PC arm versus 5.8 months (95% CI, 5.6 to 6.7 months) in the sb-PC arm. The PFS in the nab-PC arm was noninferior to PFS in the sb-PC arm (HR_{nab-PC/sb-PC} 95% CI upper bound, 1.086).

Survival

There was a 1-month increase in OS in the nab-PC versus sb-PC arm (HR, 0.922; 95% CI, 0.797 to 1.066; P = .271; Fig 2B). Median OS was 12.1 months (95% CI, 10.8 to 12.9 months) in the nab-PC arm compared with 11.2 months (95% CI, 10.3 to 12.6 months) in the sb-PC arm. The OS in the nab-PC arm was noninferior to the OS in the sb-PC arm (HR_{nab-PC/sb-PC} 95% CI upper bound, 1.066).

Analyses by Strata

Subgroup analyses for PFS and OS are presented in Figures 3A and 3B, respectively. These analyses revealed a longer but nonsignificantly different median PFS in North America in the nab-PC versus...
sb-PC arms (7.0 v 5.4 months, respectively) and in patients age ≥ 70 years (8.0 v 6.8 months, respectively; Fig 3A). Although patients enrolled in Japan and Russia/Ukraine showed no difference in OS between treatment arms, patients enrolled in North America showed increased OS when treated with nab-PC versus sb-PC (12.7 v 9.8 months, respectively; P = .008; Fig 3B). Patients younger than age 70 years showed comparable OS between treatment arms, whereas patients age ≥ 70 years in the nab-PC arm showed significantly increased OS versus those in the sb-PC arm (19.9 v 10.4 months for nab-PC v sb-PC; P = .009; Fig 3B). Sex or history did not reveal differences in survival outcomes between the two treatment arms (Figs 3A and 3B); however, there was an improvement of more than 1 month in the squamous subtype in the nab-PC arm versus sb-PC arm (median, 10.7 v 9.5 months; Figs 2C and 3B), although both arms were equally efficacious in the nonsquamous histology subtype (median, 13.1 and 13.0 months, respectively; Fig 3B).

Overall, the use and type of second-line therapy was balanced in both treatment arms. In the nab-PC arm, 53% of patients received second-line therapy compared with 54% in the sb-PC arm. The most commonly used treatments were single agents, specifically docetaxel (7%), pemetrexed (5%), erlotinib (4%), and gefitinib (3%). Twelve percent of the patients received various combination regimens. Less than 1% of patients crossed over. The median time from the end of study therapy to the start of second-line therapy was comparable in both arms (nab-PC, 31 days; sb-PC, 33 days). The use of second-line therapy was highest in Japan (85%), followed by Australia (79%), and North America (69%), and it was lowest in Russia/Ukraine (44%). Similar to the ITT population, patients who received a second-line therapy showed a nonsignificant improvement in OS favoring the nab-paclitaxel arm.

**Treatment Exposure**

The median number of cycles was 6.0 in both arms (minimum of 1, maximum of 31 in the nab-PC arm; minimum of 1, maximum of 30 in the sb-PC arm). A total of 350 patients in the nab-PC arm and 358 patients in the sb-PC arm received six or fewer cycles of treatment. The median cumulative paclitaxel dose was 1,325 mg/m² in the nab-PC arm versus 1,125 mg/m² in the sb-PC arm, with the median paclitaxel dose intensity of 82 mg/m²/wk versus 65 mg/m²/wk, respectively. The median cumulative carboplatin dose was 3,140 mg in the nab-PC arm versus 3,315 mg in the sb-PC arm, with the median carboplatin dose intensity of 166 mg/wk versus 204 mg/wk, respectively.

Of all treated patients, 46% in the nab-PC arm and 23% in the sb-PC arm had a taxane dose reduction, predominantly because of neutropenia (29% and 10%), thrombocytopenia (13% and 4%), anemia (6% and < 1%), and sensory neuropathy (2% and 6%). Despite more dose reduction in the nab-PC arm, paclitaxel dose intensity was 26% greater and cumulative dose was 18% greater for nab-PC over sb-PC. Dose delays were more common in the nab-PC arm (82%) compared with the sb-PC arm (54%). The frequency of carboplatin dose reductions, dose interruptions, and dose delays was similar to that of taxanes.

**Safety Results**

Significantly less grade ≥ 3 sensory neuropathy, neutropenia, arthralgia, and myalgia occurred in the nab-PC arm, but less thrombocytopenia and anemia occurred in the sb-PC arm (all P < .05; Table 3). Median time to improvement of grade ≥ 3 sensory neuropathy to grade 1 was 38 days in the nab-PC arm and 104 days in the sb-PC arm. Sensory neuropathy (all grades) was significantly less with nab-PC (46%) compared with sb-PC (62%; P < .001). Conversely, the percentage of patients who did not develop neuropathy was significantly higher with nab-PC (54%) versus sb-PC (38%; P < .001).

The most common nonhematologic grade ≥ 3 TRAEs with nab-PC and sb-PC were fatigue (5% and 6%, respectively), sensory neuropathy (3% and 12%), anorexia (2% and < 1%), nausea (< 1% and < 1%), myalgia (< 1% and 2%), and arthralgia (0% and 2%; Table 3). The most common hematologic grade ≥ 3 TRAEs were neutropenia (47% and 58%), leukopenia (24% and 23%), thrombocytopenia (18% and 9%), and anemia (27% and 7%). Nonhematologic and hematologic TRAEs in the first six cycles were similar to the events observed during the entire treatment period. Only 1% of patients in both arms had febrile neutropenia during this study. Two treatment-related deaths occurred, one in each arm.

Of the ITT population, 1,031 patients (98%) completed the FACT-Taxane questionnaire at baseline, and 987 (94%) had a
follow-up assessment. The mean change from baseline to final evaluation in the patient-reported FACT-Taxane scale, including a neuropathy subscale (P < .001, Figure 4), pain subscale (P < .001), and hearing loss subscale (P < .002), was significantly improved in the nab-PC versus sb-PC arm.

**DISCUSSION**

In this study, the combination of 100 mg/m² weekly nab-paclitaxel plus carboplatin AUC 6 every 3 weeks met the primary end point of ORR, demonstrating significantly improved antitumor activity compared with sb-PC (31% improvement) and was well tolerated despite higher cumulative paclitaxel dose delivered without premedication for unselected patients with NSCLC. Overall responses compared favorably with results from a phase III trial in patients with advanced NSCLC treated with sb-paclitaxel plus carboplatin. Patients with squamous cell histology responded remarkably well to treatment with nab-PC, with a 68% improvement compared with that in the sb-PC arm, which is the highest reported in a phase III study in this patient population. This is particularly intriguing because improved therapeutic options for the subset of patients with squamous histology are needed.

In general, survival in this study was comparable with historic results from trials in patients with advanced NSCLC. The combination of nab-paclitaxel plus carboplatin AUC 6 as a 3-weekly schedule in unselected patients with NSCLC resulted in a 10% improvement in PFS and OS compared with sb-PC, favoring the nab-PC arm.

Subgroup analysis revealed a trend for significantly improved OS between the study arms in patients from North America and those
who were ≥ 70 years old. Regional differences in baseline characteristics and standard of care may have played a role in the differences in survival outcomes. Advanced NSCLC is a heterogeneous disease with a relatively short survival time and thus potential regional differences should be considered when designing global clinical trials. The median OS of 19.9 months for the subgroup with an age ≥ 70 years treated with first-line nab-PC was intriguing and should be confirmed in another study. This treatment benefit in elderly patients may be related, in part, to a poorer tolerability of the every-3-week sb-PC schedule than the weekly schedule of the nab-PC arm.23 The significantly improved ORR in the squamous histology subset of patients treated with nab-PC versus sb-PC resulted in an approximately 10% improvement for OS that did not reach statistical significance, with the tails of the curves separating after 6 months through the end of the study. This late curve separation indicates a potential subgroup within this population that responds favorably to nab-PC. Studies are warranted to explore the underlying mechanism for the greater treatment benefit and potential prognostic biomarkers in the squamous subset.

Although the median cumulative taxane dose and average dose intensity were higher for nab-PC, in general, nab-PC was better tolerated, with lower rates of grade 3 and 4 neuropathy, neutropenia, arthralgia, and myalgia. Specifically, the lower incidences of neutropenia in the nab-PC arm, which were the main causes of dose delays and reductions, indicate that the higher percentage of dose delays and reduction in the nab-PC arm are likely due to the weekly versus every-3-week dosing schedule. The majority of patients treated with sb-PC (62%) and fewer than half the patients treated with nab-PC (46%) developed neuropathy during the study, and grade ≥ 3 neuropathy resolved more rapidly in the nab-PC versus sb-PC arm (38 5 104 days). This lesser rate of neuropathy was supported by the results of the FACT-Taxane tool, which showed a statistically and clinically significant reduction in the development of neuropathy symptoms, neuropathic pain in the hands and feet, and hearing loss. The relief of neuropathy-associated symptom burden may be factored into making decisions on chemotherapy options.24 Since neuropathy in some patients is irreversible with sb-PC, which has been attributed to the cremophor excipient,25,26 it is important to note that neuropathy resolved more quickly and that a significantly higher percentage of patients in the nab-PC versus sb-PC arm had no neuropathy during the study. A higher percentage of patients in the nab-PC arm developed anemia and thrombocytopenia. In the majority of patients, anemia was corrected with a single blood transfusion, and thrombocytopenia did not lead to increased rates of hemorrhages.

In conclusion, in patients with advanced NSCLC, administration of nab-PC as a first-line therapy resulted in a significantly improved ORR versus sb-PC (33% v 25%; P = .005) thereby achieving the primary end point. Nonsignificant improvement was observed in favor of the nab-PC arm for PFS or OS, meeting noninferiority criteria. The nab-PC regimen produced less severe neuropathy, neutropenia, myalgia, and arthralgia compared with sb-PC. The increased risk of thrombocytopenia and anemia in the nab-PC regimen was readily manageable. Taken together, the nab-PC regimen has a favorable risk-benefit profile compared with that of sb-PC as first-line therapy for all patients with NSCLC.

### Table 3. Most Common Treatment-Related Grade ≥ 3 AEs According to NCI-CTCAE

<table>
<thead>
<tr>
<th>AE</th>
<th>nab-PC (%)</th>
<th>sb-PC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 3</td>
<td>Grade 4</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>33</td>
<td>14</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>13</td>
<td>5</td>
</tr>
<tr>
<td>Anemia</td>
<td>22</td>
<td>5</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>&lt; 1</td>
<td>&lt; 1</td>
</tr>
</tbody>
</table>

Abbreviations: AE, adverse event; nab-PC, 130-nm albumin-bound paclitaxel + carboplatin; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; N/S, not significant; sb-PC, solvent-based paclitaxel+ carboplatin.

*P < .05 in favor of nab-PC.
†P < .05 in favor of sb-PC.

### Authors’ Disclosures of Potential Conflicts of Interest

Although all authors completed the disclosure declaration, the following author(s) indicated a financial or other interest that is relevant to the subject matter under consideration in this article. Certain relationships marked with a “U” are those for which no compensation was received; those relationships marked with a “C” were compensated. For a detailed description of the disclosure categories, or for more information about ASCO’s conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors.

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**Honoraria:** None

**Research Funding:** Mark A. Socinski, Celgene; Igor Bondarenko, Celgene; Nina A. Karaseva, Celgene; Anatoly M. Makhson,
Provision of study materials or patients: Mark A. Socinski
Collection and assembly of data: Mark A. Socinski, Igor Bondarenko, Nina A. Karaseva, Anatoly M. Makhsan, Igor Vynnychenko, Isamu Okamoto, Jeremy K. Hon, Vera Hirsh, Markus F. Renschler
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REFERENCES


Acknowledgment
We thank Rutia Slepetis, Celgene, for coordination of the clinical trial sites and Anita N. Schmid, PhD, Celgene, for expert medical writing assistance. The authors are fully responsible for content and editorial decisions for this article.