Treatment of metastatic breast cancer with *nab*-paclitaxel in the community practice setting: a US Oncology survey

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Background Different dosages-schedules of nab-paclitaxel have been assessed in trials of metastatic breast cancer (MBC). However, there is limited information on nab-paclitaxel dosing-scheduling in the community setting.
Objective To report on experience with nab-paclitaxel for human epidermal growth factor receptor 2 (HER2)–negative MBC and identify patient characteristics affecting nab-paclitaxel treatment patterns in the community practice setting.
Methods From September 6-October 21, 2013, a 35-question, web-based survey on nab-paclitaxel dosing, toxicities leading to dose modifications, management, and treatment duration was sent to US Oncology network oncologists. Respondents were categorized by percentage of their patients with HER2-negative MBC who received nab-paclitaxel.
Results 104 of 428 oncologists responded; 84% were from large practices (≥16 oncologists), and 56% had a high level of experience using nab-paclitaxel. For first- and second-line treatment, 100 mg/m2 weekly was the most common starting dosage-schedule, followed by 125 mg/m2 weekly and 260 mg/m2 every 3 weeks (q3w); 150 mg/m2 weekly was used least frequently. Several factors, including select aggressive disease characteristics, were found to affect nab-paclitaxel dose selection. Weekly dosing was preferred in patients with select aggressive disease characteristics, whereas q3w dosing was commonly used in patients aged ≤50 years and those with good performance status. Differences in management styles among oncologists with high compared with infrequent nab-paclitaxel experience were also observed. Peripheral neuropathy and neutropenia were common dose-limiting toxicities.
Limitations Recall and response bias may be limitations of this study.
Conclusions In the community setting, nab-paclitaxel 100 mg/m2 weekly was the most commonly used starting dose for patients with HER2-negative MBC, including those with aggressive disease characteristics.
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Death rates of patients with breast cancer have declined over the past decade.[1] In 2015, although it is estimated that 231,840 new cases of female breast cancer will be diagnosed, there will be about 40,000 deaths from breast cancer.[2] Improvements in therapeutic and screening options for patients with breast cancer have contributed to this trend. Although the 5-year survival rate for metastatic breast cancer (MBC) is 25%, it is nearly 99% in patients with localized disease.[1] Human epidermal growth factor receptor 2 (HER2) overexpression occurs in about 15%-25% of patients with breast cancer, meaning that patients who are negative for HER2 represent the majority of patients with MBC.[3,4] Chemotherapy remains an important option for the treatment of HER2-negative MBC.

nab-Paclitaxel is an albumin-bound formulation of paclitaxel designed to enhance the drug's clinical activity and improve its safety profile compared with taxanes formulated in chemical solvents.[5] The safety and efficacy of *nab*-paclitaxel have been characterized in patients with MBC in several clinical trials.[5-8] A phase 3 study demonstrated a favorable safety profile and significant improvement in overall response rate (ORR, the primary endpoint), as well as time to tumor progression for patients with MBC receiving *nab*-paclitaxel compared with paclitaxel in the first- or second-line or higher settings.[5] The median overall survival (OS) in patients receiving second-line or higher therapy was significantly longer for patients receiving *nab*-paclitaxel compared with paclitaxel. These findings led to the approval by the US Food and Drug Administration of *nab*-paclitaxel 260 mg/m^2 every 3 weeks (q3w) for the treatment of metastatic breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy.[9] Prior therapy should have included an anthracycline unless clinically contraindicated.

To date, no phase 3 trial has evaluated different doses-schedules of *nab*-paclitaxel as have been done

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for paclitaxel and docetaxel in patients with MBC.[10,11] However, a phase 2 study evaluated different doses and schedules of *nab*-paclitaxel compared with docetaxel as first-line treatment for patients with MBC.[6,7] The trial demonstrated a trend toward improved median OS with various doses of *nab*-paclitaxel and docetaxel in patients with MBC treated in the first line. Based on independent review, *nab*-paclitaxel at a dose-schedule of 100 mg/m^2 weekly and 150 mg/m^2 weekly demonstrated the longest median progression-free survival (PFS; 12.8 and 12.9 months, respectively) compared with docetaxel (7.5 months) and *nab*-paclitaxel 300 mg/m^2 q3w (11.0 months), with an overall *P* value of .0498. Median OS was longest with *nab*-paclitaxel 150 mg/m^2 weekly (33.8 months) compared with all other arms in the study (22.2-27.7 months), with an overall *P* value of .047; however, the 150-mg/m^2 weekly dose-schedule was associated with a higher rate of adverse events (AEs) compared with other doses-schedules of *nab*-paclitaxel, as well as a higher rate of dose reductions.[7] Subsequently, a phase 3 trial conducted by the Cancer and Leukemia Group B (CALGB 40502) compared the following treatment combinations in patients with HER2-negative MBC: *nab*-paclitaxel 150 mg/m^2 weekly plus bevacizumab 10 mg/kg every 2 weeks (q2w); paclitaxel 90 mg/m^2 for the first 3 of 4 weeks (qw 3/4) plus bevacizumab 10 mg/kg q2w; and ixabepilone 16 mg/kg qw 3/4 plus bevacizumab 10 mg/kg q2w.12 A preliminary analysis from the trial reported a similar median PFS (primary endpoint) for the *nab*-paclitaxel and paclitaxel arms (9.2 vs 10.6 months, respectively; hazard ratio [HR], 1.19; 95% confidence index [CI], 0.96-1.49; *P* = .12) but high rates of grade 3 or higher toxicities, including sensory neuropathy, leukopenia, neutropenia, and fatigue, in the *nab*-paclitaxel plus bevacizumab arm. Frequent dose reductions in the *nab*-paclitaxel plus bevacizumab arm further suggested that the 150-mg/m^2 weekly schedule of *nab*-paclitaxel in combination with bevacizumab may not have been ideal.

Clinical trial data may not be translatable to the community setting, in which patient characteristics, comorbidities, and experience with specific agents vary greatly. Therefore, this survey was conducted to understand real-world experience with respect to dosing-scheduling of *nab*-paclitaxel among oncologists in the US Oncology network for the treatment of patients with HER2-negative MBC. In addition, the impact of *nab*-paclitaxel experience (high vs infrequent use) on treatment strategies used by oncologists and the use of *nab*-paclitaxel in patients with aggressive disease features were examined.

Methods

A web-based survey containing 35 questions was sent to US Oncology network oncologists (universe of potential respondents, N = 428) between September 6, 2013 and October 21, 2013. Questions included those related to *nab*-paclitaxel schedule (eg, weekly [days 1, 8, and 15 of a 4-week cycle] and q3w), dosing (eg, 100, 125, and 150 mg/m^2), use as monotherapy or in combination, common reasons for discontinuations, and common AEs leading to dose modifications (online material). Respondents were classified as having high or infrequent experience with *nab*-paclitaxel if ≥33% or <33% of their patients with HER2-negative MBC were receiving *nab*-paclitaxel, respectively.

Data distribution for oncologists with high or infrequent *nab*-paclitaxel experience was inspected for normality and homogeneity of variance, which included examination of box plots, skewness, and standard deviation (SD) measures. The Welch 2-sample *t* test was used to assess differences between both group means, accounting for the possibility of unequal variances among the groups. A 2-sample test for equality of proportions was used to assess whether the 2 groups had equal or different proportions.

Results

Respondent demographics

In total, 104 US Oncology oncologists responded to the survey. The demographics of the responding oncologists are shown in Table 1. Most oncologists (84%) were from large practices with a pharmacist present. More than half (56%; n = 58) of the oncologists were considered to have a high level of experience with *nab*-paclitaxel. On average, oncologists with a high level of experience with *nab*-paclitaxel were in practice for a shorter amount of time compared with those with infrequent experience (mean, 15.3 vs 18.4 years, respectively). The mean overall number of unique patients with HER2-negative MBC who were treated between January 2010 and June 2013 was significantly higher among oncologists with infrequent experience of using the drug compared with those with high experience (*P* = .001). However, the number of unique patients with HER2-negative MBC who were treated with *nab*-paclitaxel during this time frame was significantly lower among oncologists with infrequent compared with high experience (*P* = .001). The mean ratio of *nab*-paclitaxel–treated patients to patients with HER2-negative MBC was 0.43 and was numerically higher in the group with a high level of *nab*-paclitaxel experience.

Dose-schedule

The most common starting dose-schedule was weekly *nab*-paclitaxel 100 mg/m^2 in both the first- and second-line treatment of patients with HER2-negative MBC (Table 2). The other doses used in the first line by order of preference included 125 mg/m^2 weekly, 260 mg/m^2 q3w, and ≤90 mg/m^2 weekly. In the second line, ≤90 mg/m^2 weekly was the second most commonly used starting dose, followed by 125 mg/m^2 weekly and 260 mg/m^2 q3w. Overall, 150 mg/

TABLE 1 Responding oncologist demographics

Demographic	Facility size, sm, med, lg[b]	Pharmacist in practice, yes/no	Oncologist experience with use of *nab*-paclitaxel[a]		Total (N = 104)
			High (n = 58)	Infrequent (n = 46)	
Practice location[c]					
South	0, 2, 5	5/2	39	26	65
West	0, 0, 4	4/0	10	10	20
Midwest	1, 2, 1	3/1	9	8	17
Northeast	0, 0, 1	1/0	0	2	2
Other demographics					
Mean no. of years in practice since residency	—	—	15.3	18.4	16.7
Mean no. of unique patients with HER2-negative MBC Jan 2010-June 2013	—	—	8.9	14.5[d]	11.4
Mean no. of unique patients with HER2-negative MBC treated with *nab*-paclitaxel Jan 2010-June 2013	—	—	5.1[d]	2.2	3.8
Mean ratio (*nab*-paclitaxel patients or patients with HER2-negative MBC)	—	—	0.64	0.17	0.43

HER2, human epidermal growth factor receptor 2; MBC, metastatic breast cancer

[a]Respondents were classified as having high or infrequent experience with *nab*-paclitaxel if ≥ 33% or < 33% of their patients with HER2-negative MBC were receiving *nab*-paclitaxel, respectively. [b]Practice size definitions: small, 1-5 medical oncologists; medium, 6-15 medical oncologists; large, ≥16 medical oncologists. [c]US Census regions. [d]$P = .001$.

TABLE 2 Starting dose of *nab*-paclitaxel by experience level and line of therapyab

Dose-schedule	First line, %			Second line, %		
	High (n = 58)	Infrequent (n = 46)	Total (N = 104)	High (n = 58)	Infrequent (n = 46)	Total (N = 104)
≤90 mg/m² qw	9	9	9	19	20	19
100 mg/m² qw	53	48	51	52	65	58
125 mg/m² qw	26	17	22	19	9	14
150 mg/m² qw	3	4	4	3	0	2
260 mg/m² q3w	9	22	14	7	7	7

HER2, human epidermal growth factor receptor 2; MBC, metastatic breast cancer; qw, weekly (the first 3 of 4 weeks); q3w, every 3 weeks

[a]Question, *For first- or second-line therapy, on which dose and schedule of nab-paclitaxel are you most likely to start your HER2-negative MBC patients? Select one.* [b]Respondents were classified as having high or infrequent experience with *nab*-paclitaxel if ≥33% or <33% of their patients with HER2-negative MBC were receiving *nab*-paclitaxel, respectively.

m² weekly was reported as the least frequently used in the first- and second-line settings.

Patients with aggressive disease features were defined by 1 or more of the following: 50 years or older at diagnosis, triple-negative breast cancer (TNBC), short disease-free interval (DFI), predominant visceral metastases, or comorbidities and/or poor performance status. Oncologists chose 100 mg/m² weekly as the most common starting dose-schedule of single-agent *nab*-paclitaxel across all of the aggressive disease features (Table 3). The second most common dose varied by aggressive disease feature – 125 mg/m² weekly for patients with TNBC, short DFI, and predominant visceral metastases, and ≤90 mg/m² weekly for patients with comorbidities and/or poor performance status. For patients aged ≤50 years at diagnosis, the 260-mg/m² q3w dose was the second most common dose chosen.

Patient characteristics and *nab*-paclitaxel use

The most important patient factors affecting the oncologists' decision to use *nab*-paclitaxel monotherapy for patients with HER2-negative MBC were comorbidities and/or poor performance status (82%) and quality of

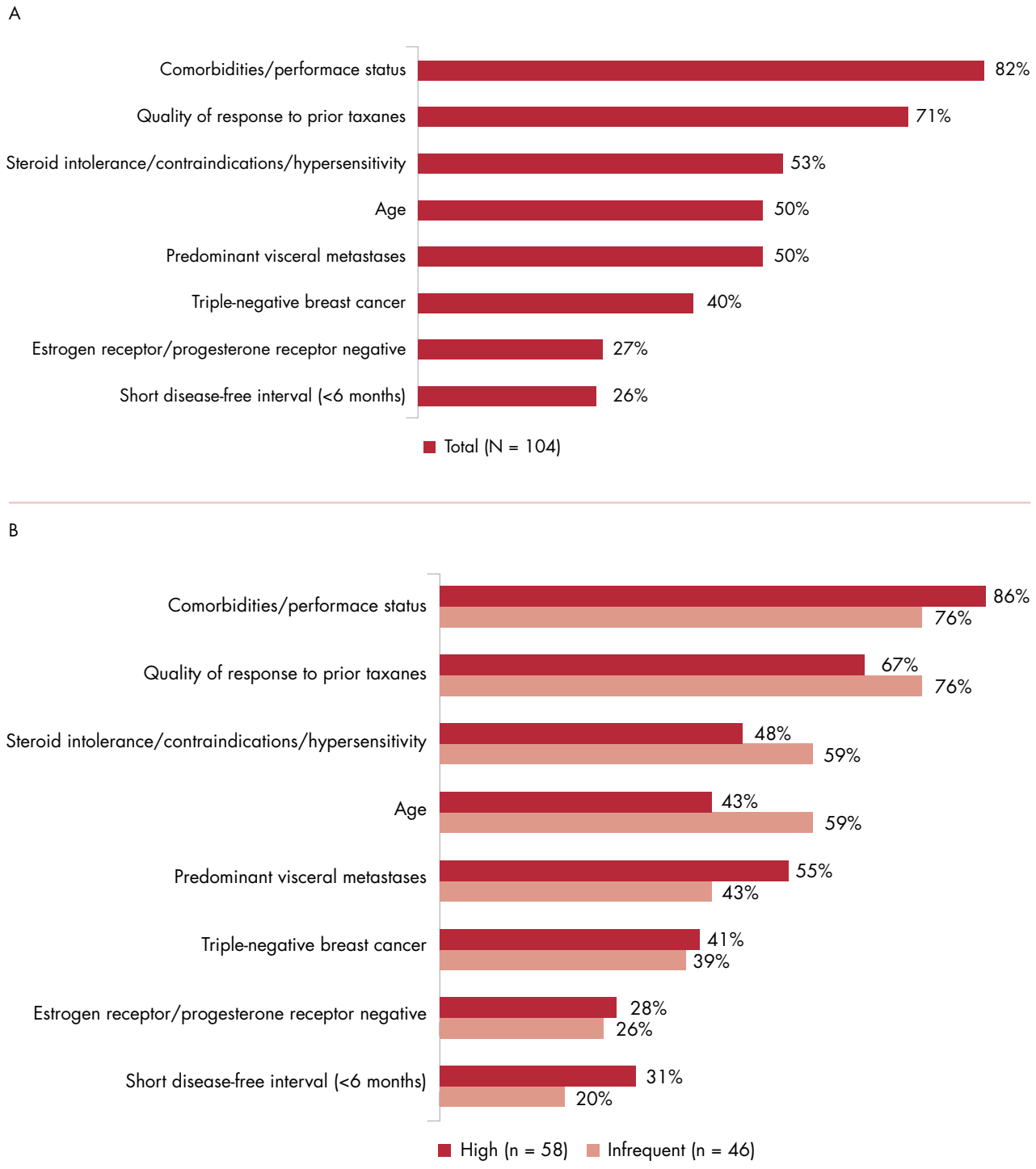

FIGURE 1 Patient and disease characteristics affecting the decision to use *nab*-paclitaxel

Overall (A) and user group (B) responses to the following question: *What are the most important clinical factors affecting your decision to use nab-paclitaxel monotherapy for HER2-negative MBC patients? Choose the top 4 most important factors.* HER2, human epidermal growth factor receptor 2; MBC, metastatic breast cancer. Respondents were classified as having high or infrequent experience with *nab*-paclitaxel if ≥33% or <33% of their patients with HER2-negative MBC were receiving *nab*-paclitaxel, respectively.

TABLE 3 Dose-schedule of *nab*-paclitaxel in patients with aggressive disease characteristics

Dose-schedule	50 y or older at diagnosis, %	TNBC, %	Short DFI (<6 mo), %	Predominant visceral metastases, %	Comorbidities/ poor PS, %
≤90 mg/m^2 qw	4	5	6	6	35
100 mg/m^2 qw	**34**	**36**	**35**	**38**	**49**
125 mg/m^2 qw	24	**27**	**26**	**28**	10
150 mg/m^2 qw	9	12	12	10	3
260 mg/m^2 q3w	**29**	20	19	19	3

DFI, disease-free interval; PS, performance status; qw, weekly (the first 3 of 4 weeks); q3w, every 3 weeks; TNBC, triple-negative breast cancer

[a]Question: *Which dose-schedule of* nab*-paclitaxel monotherapy are you most likely to use in patients with the following aggressive metastatic disease features? Select one.*

Bold/underline, dose-schedule selected most often. Bold, dose-schedule selected second most often.

response to prior taxanes (71%; Figure 1A). Additional factors that influenced the decision to use *nab*-paclitaxel monotherapy were steroid intolerance, contraindications, or hypersensitivity; age; and/or predominant visceral metastases. Factors such as TNBC, short DFI, and hormone-receptor status (estrogen or progesterone receptor negative) ranked lowest among those influencing choice of *nab*-paclitaxel dose-schedule.

Oncologists reported that, on average, nearly half (median, 50%) of their HER2-negative patients who received taxanes for the treatment of early-stage disease subsequently received *nab*-paclitaxel in the MBC setting. Oncologists with a high level of *nab*-paclitaxel experience reported a significantly higher proportion of HER2-negative patients with subsequent *nab*-paclitaxel use in the MBC setting compared with infrequent *nab*-paclitaxel users (55% vs 36%; $P = .001$).

Overall, 62% of oncologists indicated that they used *nab*-paclitaxel in combination with other agents in patients who were negative for HER2; combinations with *nab*-paclitaxel were reportedly used in about 25% of these patients. Carboplatin was the most common *nab*-paclitaxel combination partner, and when used in combination, the 100-mg/m^2 weekly dose of *nab*-paclitaxel was most often chosen.

Dose-limiting toxicities

On average, oncologists estimated that about 29% of their patients with HER2-negative MBC who were receiving *nab*-paclitaxel experienced dose-limiting peripheral neuropathy. The reported incidence of peripheral neuropathy decreased as the dose of *nab*-paclitaxel decreased (Table 4). About half of all oncologists (49%) indicated that dose-limiting peripheral neuropathy occurred most commonly with the 260-mg/m^2 q3w dose-schedule of *nab*-paclitaxel, and 27% of all oncologists indicated that dose-limiting peripheral neuropathy occurred most commonly with the 150-mg/m^2 weekly dose-schedule. Nearly half (45%) of all oncologists indicated that peripheral neuropathy typically occurred >12 weeks after the initiation of treatment. More than 50% of oncologists indicated that, following dose reduction/discontinuation of *nab*-paclitaxel, resolution of peripheral neuropathy occurred at >6 weeks. Similarly, dose-limiting neutropenia was reported to be associated with higher doses of *nab*-paclitaxel, with 48% and 36% of oncologists reporting dose-limiting neutropenia with the 260-mg/m^2 q3w and 150-mg/m^2 weekly doses, respectively.

Management strategies

Overall, oncologists indicated that about 30% of patients receiving *nab*-paclitaxel required dose and/or schedule changes. Patients remained on *nab*-paclitaxel therapy for a mean of 20 and 23 weeks (median, 17 and 24 weeks) before discontinuing due to AEs and disease progression, respectively. The majority (76%) of oncologists reported that dose-limiting peripheral neuropathy was the most common safety-related reason for discontinuation of *nab*-paclitaxel, followed by dose-limiting neutropenia, which was reported by 19% of oncologists. The initial modification strategy practiced by most oncologists was to reduce dose but maintain the schedule (71% of oncologists). The next modification strategy was to either dose delay or skip (34%) or change both dose and schedule (35%).

Impact of physician experience

Differences were noted in *nab*-paclitaxel dose-schedule preference and management strategies for dose modification/reduction when respondents were stratified by level of *nab*-paclitaxel experience (Table 2 and Figure 1B). With respect to *nab*-paclitaxel dose-schedule, 125 mg/m^2 weekly was used more frequently by oncologists with a high level of *nab*-paclitaxel experience compared in the first-line setting with a low level of experience (26% vs 17%, respectively) and in the second-line setting (19% vs 9%). In con-

trast, the 260-mg/m^2 q3w dose-schedule was used more often in the first-line setting by oncologists with infrequent *nab*-paclitaxel experience compared with those with a high level of experience (22% vs 9%). Of note, 100 mg/m^2 weekly was the most common starting dose-schedule regardless of level of *nab*-paclitaxel experience. Those with high *nab*-paclitaxel experience also reported longer use of *nab*-paclitaxel before discontinuation due to AEs compared with those with infrequent experience (about 3.5 weeks difference; P = .042).

TABLE 4 *nab*-Paclitaxel dose-schedule associated with dose-limiting peripheral neuropathy[a]

nab-Paclitaxel dose/schedule	Oncologist experience with use of *nab*-paclitaxel,[b] n (%)		
	High (n = 58)	Infrequent (n = 46)	Total (n = 104)
≤ 90 mg/m2 qw	1 (2)	1 (2)	2 (2)
100 mg/m2 qw	0 (0)	2 (4)	2 (2)
125 mg/m2 qw	14 (24)	6 (13)	20 (19)
150 mg/m2 qw	14 (24)	14 (30)	28 (27)
260 mg/m2 q3w	29 (50)	22 (48)	51 (49)

qw, weekly (the first 3 out of 4 weeks); q3w, every 3 weeks

[a]Question: *In your clinical experience, which dose and schedule of nab-paclitaxel is most commonly associated with dose-limiting neuropathy? Select one.* [b]Respondents were classified as having high or infrequent experience with *nab*-paclitaxel if ≥33% or <33% of their patients with HER2-negative MBC were receiving *nab*-paclitaxel, respectively.

When considering patient disease characteristics, oncologists with high *nab*-paclitaxel experience reported comorbidities and/or poor performance status and quality of response to prior taxanes as the most important criteria for selecting dose-schedule of *nab*-paclitaxel, followed by the presence of predominantly visceral metastases. For this group of respondents, *nab*-paclitaxel 100 mg/m^2 weekly was selected most commonly across all 5 aggressive disease features. With respect to management strategies, oncologists with high *nab*-paclitaxel experience generally chose to dose delay or skip a dose and then change both the dose and schedule after the initial dose reduction of *nab*-paclitaxel.

Similar to the high-experience group, comorbidities and/or poor performance status and quality of response to prior taxanes were the primary disease characteristic criteria reported for selecting dose-schedule among oncologists with infrequent *nab*-paclitaxel experience. In contrast to the high experience group, steroid intolerance and age were also important criteria for oncologists with infrequent *nab*-paclitaxel experience. With respect to dose in patients with aggressive disease features, oncologists with infrequent *nab*-paclitaxel experience also reported use of 100 mg/m^2 weekly across most aggressive disease features but chose 125 mg/m^2 weekly most often for patients with predominant visceral metastases and 260 mg/m^2 q3w for patients aged 50 years or older at diagnosis. After the initial dose reduction of *nab*-paclitaxel, oncologists with infrequent *nab*-paclitaxel experience generally changed both the dose and the schedule, followed by either dose delay or skipping a dose.

Discussion

This is the first account of physician-reported use of *nab*-paclitaxel for the treatment of HER2-negative MBC in the US community practice setting. The results revealed differences in doses-schedules used by oncologists in the community setting and those used in clinical trial settings. This survey demonstrated that in the community practice setting in the United States, *nab*-paclitaxel 100 mg/m^2 weekly was the most commonly used starting dose-schedule for patients with HER2-negative MBC in the first- and second-line settings. This dose was chosen most often regardless of patient age or disease characteristics.

The approved dose-schedule of *nab*-paclitaxel in the treatment of MBC is 260 mg/m^2 q3w, which was assessed in a phase 3 trial of patients with MBC.[5,9] However, many other doses-schedules have also been studied in clinical trials of patients with MBC.[6,12] In this report, in the community setting, *nab*-paclitaxel 100 mg/m^2 weekly was reported to be used most commonly. One of the key attributing factors affecting dose-schedule choice in the community setting seemed to be toxicities. Higher rates of neutropenia and peripheral neuropathy were observed with higher doses of *nab*-paclitaxel (≥150 mg/m^2) by community oncologists in this survey. These results are in accordance with those observed in the phase 2 trial in patients with MBC, in which the 100-mg/m^2 weekly dose of *nab*-paclitaxel demonstrated a lower incidence of neutropenia and peripheral neuropathy (all-grade as well as grade 3 or 4) compared with the 150-mg/m^2 weekly dose-schedule.6 Preliminary results from the CALGB 40502 study revealed that, despite demonstrating a similar median PFS, bevacizumab in combination with *nab*-paclitaxel 150 mg/m^2 weekly compared with bevacizumab in combination with paclitaxel 90 mg/m^2 weekly was associated with higher rates of grade 3 or 4 sensory neuropathy (25% vs 16%; P = .012) and neutropenia (47% vs 18%; P = .0001), as well as a higher incidence of dose modifications.12 Thus, the addition of bevacizumab to weekly *nab*-paclitaxel 150 mg/m^2 may not be feasible in patients with MBC.

Patient characteristics seemed to play a role in the deci-

sion to use *nab*-paclitaxel monotherapy. Comorbidities and/or poor performance status, quality of response to prior taxanes, age, and predominant visceral metastases were the most common patient and disease characteristics that had an impact on the decision to use *nab*-paclitaxel monotherapy. The steroid intolerance, contraindications, or hypersensitivity category was also selected by more than half of the oncologists in this study as a key important clinical factor affecting their decision to use *nab*-paclitaxel monotherapy. This is not surprising because the albumin formulation of *nab*-paclitaxel alleviates the need for steroid premedication and is associated with a low incidence of hypersensitivity reactions.[9]

Although 100 mg/m^2 was the most commonly reported starting dose for *nab*-paclitaxel in patients with HER2-negative MBC, the 125-mg/m^2 dose of *nab*-paclitaxel was reportedly used more frequently in patients with HER2-negative MBC with aggressive disease characteristics, including TNBC, short DFI, and predominant visceral metastases, compared with the general population of patients with HER2-negative MBC. These results suggest that oncologists treat aggressive disease more intensively. Results of a recent phase 2 study of patients with metastatic TNBC revealed that weekly *nab*-paclitaxel plus carboplatin and biweekly bevacizumab was effective, resulting in a 9.2-month median PFS, a clinical benefit rate of 94%, and an ORR of 85%.13 Fatigue and neutropenia were the most common all-grade AEs observed in the study. The incidence of grade 3 or 4 neutropenia was 53%, and the incidence of grade 3 or 4 peripheral neuropathy was low (6%). The phase 2/3 tnAcity trial (ClinicalTrials.gov NCT01881230) that is currently assessing *nab*-paclitaxel (125 mg/m^2 weekly) in combination with carboplatin or gemcitabine in patients with metastatic TNBC will provide further insight into the efficacy and safety of *nab*-paclitaxel regimens in this patient subset. A retrospective analysis of phase 2 and 3 trials of *nab*-paclitaxel in patients with MBC also confirmed its efficacy in patients with short DFI and predominant visceral metastases.[14] Similar efficacy and safety outcomes with *nab*-paclitaxel were observed in these patient subsets and the intent-to-treat population of each trial. In addition, patients with predominant visceral metastases or short DFI treated with *nab*-paclitaxel had a higher ORR compared with those treated with docetaxel and paclitaxel. Taken together, these findings support the use of *nab*-paclitaxel in patients with aggressive disease characteristics.

In this study, a clear pattern emerged with respect to candidates for weekly compared with q3w dosing of *nab*-paclitaxel. "Fit" patients, including those with good performance status, younger age, and no comorbidities, were identified as being good candidates for q3w therapy, whereas those with a history of peripheral neuropathy, pretreatment, steroid intolerance, or comorbidities, as well as older patients, were identified as being good candidates for weekly therapy. These findings are likely related to the fact that fit candidates for *nab*-paclitaxel q3w are more able to tolerate a higher dose of *nab*-paclitaxel per infusion. These assumptions are supported by findings from the phase 2 trial of various doses-schedules of *nab*-paclitaxel compared with docetaxel in patients with MBC.[6,7] In that study, for patients receiving *nab*-paclitaxel 300 mg/m^2 q3w compared with 100 mg/m^2 weekly, the rate of grade 3 or 4 neutropenia was significantly higher (P = .011), and rates of grade 3 or 4 sensory neuropathy were numerically higher. Patients who received *nab*-paclitaxel 300 mg/m^2 q3w also had a shorter duration of treatment (median, 22 weeks) compared with those receiving *nab*-paclitaxel 100 mg/m^2 weekly (median, 30 weeks), suggesting that the higher dose at the q3w schedule was less tolerable than the 100-mg/m^2 weekly dose-schedule.

In this survey, oncologists reported that slightly more than a quarter of their patients experienced dose-limiting peripheral neuropathy. Most oncologists reported that development of dose-limiting peripheral neuropathy was less frequent with doses of 100 mg/m^2 weekly or ≤90 mg/m^2 weekly (2% for each). In addition, peripheral neuropathy was generally reported to occur >12 weeks after initiation of treatment, in line with reports from clinical trials. The time to onset of neuropathy in the phase 2 trial ranged from 22 to 27 weeks in the *nab*-paclitaxel arms.[7] About a third of respondents reported that peripheral neuropathy resolved or improved between 4 and 6 weeks after dose reduction/discontinuation, and about half of them reported that it took more than 6 weeks. In both the phase 2 and phase 3 trials of *nab*-paclitaxel, the median time to improvement in peripheral neuropathy was about 1 month.[5,7] Again, differences in peripheral neuropathy assessment and reporting may play a role in this. The safety profile of *nab*-paclitaxel schedules observed in this survey is generally in line with results from the phase 2 and 3 trials; however, because of differences in methodology, percentages cannot be compared directly.

It is also interesting to note that management strategies, such as dose modifications, differed among oncologists with different levels of experience with *nab*-paclitaxel. This may have played a role in the length of time patients stayed on treatment because oncologists with a high level of experience with *nab*-paclitaxel reported slightly longer periods of time before discontinuation of *nab*-paclitaxel therapy compared with those with infrequent experience. In addition, patients treated in the community setting are often different than those in clinical trial settings. Patients in clinical trial settings are heavily selected to fit within the inclusion criteria of the trials. Furthermore, social factors may place patients in the weekly or q3w category irrespective of their health status. For example, younger patients

may prefer to be treated q3w because the schedule may be more convenient for their active lifestyles.

This study was limited to US Oncology network oncologists. A limitation of this study, as is the case with any type of survey, is the potential of a response bias. Recall bias is another potential limitation. The sample size of 104 respondents also limits interpretation of the results. The amount of data regarding combination therapy with *nab*-paclitaxel was, unfortunately, too small to draw conclusions.

In summary, the results of this survey indicated prevalent use of the 100-mg/m^2 weekly *nab*-paclitaxel dose-schedule in patients with HER2-negative MBC, including those with aggressive disease characteristics in the community practice setting. Peripheral neuropathy was considered to be the most common safety-related reason for discontinuation of *nab*-paclitaxel therapy. Differences in management strategies among oncologists with different levels of experience with *nab*-paclitaxel were noted, suggesting that dose and schedule decisions are reflective of both patient characteristics and physician experience.

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