A Phase II Trial of Older Adults With Metastatic Breast Cancer Receiving *nab*-Paclitaxel: Melding the Fields of Geriatrics and Oncology

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Abstract

***nab*-Paclitaxel may be an attractive therapy for older adults because of its efficacy, the infrequency of allergic reactions, and the lack of need for steroid pre-medications. We evaluated the tolerability and efficacy of *nab*-paclitaxel in older adults with metastatic breast cancer, as well as the relationship between a geriatric assessment-based toxicity risk score and chemotherapy toxicity, dose reductions, dose delays, and hospitalizations. Patients with intermediate/high toxicity risk scores had higher risk of grade ≥ 3 toxicity than those with low risk scores, and a higher mean risk score was associated with higher likelihood of dose reductions and hospitalizations. A geriatric assessment-based risk score can help weigh the risks and benefits of chemotherapy in older adults, and should be incorporated into future trials testing new therapies in this population.**

Introduction: Phase II clinical trials including geriatric assessment (GA) measures are critical for improving the evidence base for older adults with cancer. We assessed the efficacy and tolerability of *nab*-paclitaxel in older adults with metastatic breast cancer (MBC). **Patients and Methods:** Patients aged ≥ 65 years with MBC and ≤ 1 previous line of chemotherapy received 100 mg of *nab*-paclitaxel on days 1, 8, and 15 of a 28-day cycle. A GA was completed pre-chemotherapy, and the validated Cancer and Aging Research Group (CARG) chemotherapy toxicity risk score was calculated. Relationships between tolerability (number of courses, hospitalizations, dose reductions, and toxicity) and risk score were assessed using general linear models, Student *t* tests, and the Fisher test. Response rate and progression-free survival were evaluated using the Kaplan-Meier method. **Results:** Forty patients (mean age, 73 years; range, 65-87 years) were included. The median number of cycles was 6, 75% (n = 30) of patients had ≥ 1 dose hold, and 50% (n = 20) had ≥ 1 dose reduction. Fifty-eight percent (n = 23) had treatment-related ≥ grade 3 toxicities, and 30% (n = 12) were hospitalized owing to toxicity. Thirty-five percent (n = 14) responded, and the median progression-free survival was 6.5 months (95% confidence interval, 5.5 months to undefined). Patients with intermediate/high toxicity risk scores had higher risk of grade ≥ 3 toxicity than those with low risk scores (odds ratio, 5.8; 95% confidence interval, 1.3-33.1; $P = .01$). A higher mean risk score was associated with higher likelihood of dose reductions and hospitalizations. **Conclusions:** Among older adults with MBC receiving weekly *nab*-paclitaxel, more than one-half experienced ≥ grade 3 chemotherapy toxicity. However, a GA-based risk score could predict treatment tolerability.

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Introduction

Breast cancer is a disease associated with aging,[1] and almost one-half of breast cancer diagnoses occur in women age 65 and older.[2] However, older adults with breast cancer have been underrepresented in registration clinical trials that inform the recommended drug dosing and expected toxicity profiles, which is included within the package insert.[3,4] Furthermore, little is known about whether older adults included in clinical trials are representative of the general population, because geriatric assessment (GA) measures are not included.[5] In order to improve the evidence base for treatment of older adults with cancer, the Institute of Medicine, the American Society for Clinical Oncology, and the Cancer and Aging Research Group (CARG)[6] have identified phase II clinical trials including GA measures as a critical component to improve the evidence base for treating older adults with cancer.[7,8]

A recent systematic review identified only 16 phase II trials focusing on older patients treated with chemotherapy for metastatic breast cancer published between 2001 and 2014.[9] Yet most of these studies did not include geriatric-specific evaluations, and patients were enrolled based on chronologic age alone. Factors besides chronologic age may affect treatment tolerance in older patients, and a more detailed evaluation is warranted.[10] This evaluation is known as the GA, and it measures a patient's functional status, comorbidities, cognition, nutritional status, social support, and psychological state.[11] There is an abundance of information demonstrating that GA detects general health care problems in older patients with cancer that routinely are underrecognized in clinical oncology care.[12] Furthermore, in older patients with cancer, the GA has been shown to predict both survival[13-17] and severe chemotherapy toxicity.[18-22] The CARG chemotherapy toxicity calculator, which utilizes data from the GA, was developed and validated in 750 older adults with solid tumors receiving chemotherapy, and has been shown to predict grade 3-5 chemotherapy toxicity more accurately than currently used measures such as the Karnofsky performance status.[18,19]

Current guidelines list weekly taxanes among the preferred options for treating older adults with metastatic breast cancer.[23] Nanoparticle albumin-bound (*nab*) paclitaxel has proven to be an efficacious and safe alternative to solvent-based taxanes (such as paclitaxel and docetaxel), because it requires no premedication and has a lower rate of hypersensitivity reactions.[24] Although retrospective studies have shown that *nab*-paclitaxel appears to be safe in older adults,[25] its clinical benefit and tolerability have not been prospectively assessed.

In this study, we evaluated the efficacy and the tolerability of weekly *nab*-paclitaxel in older adults with metastatic breast cancer. Furthermore, we explored the use of a previously developed and validated GA-based risk score (CARG Chemotherapy Toxicity Calculator)[18,19] to predict the need for dose reductions, dose delays, hospitalizations, and/or grade 3 to 5 chemotherapy toxicity attributed to treatment.

Materials and Methods

Study Design and Objectives

This was a phase II, single-arm, open-label, clinical trial of *nab*-paclitaxel in older adults with metastatic breast cancer conducted at City of Hope National Medical Center in Duarte, CA and Ohio State University Cancer Center in Columbus, OH. The primary objective was to assess tolerability, defined as the presence of grade 2 to 5 chemotherapy toxicity, and dose reductions, delays, or interruptions. Secondary objective included estimation of overall response rate (ORR, defined as the sum of complete and partial response), median progression-free survival [PFS], median overall survival (OS), the use of a cancer-specific GA to describe the study population, and the CARG chemotherapy toxicity calculator to predict the need for dose reduction, dose delays, or occurrence of grade 3 to 5 chemotherapy toxicity. This study was approved by the City of Hope National Medical Center Institutional Review Board and all study participants provided written informed consent. The study was registered at clinicaltrials.gov (NCT01463072).

Eligibility

Patients were eligible if they were age $\geq$ 65 years, had a diagnosis of metastatic breast cancer with any hormone receptor or human epidermal growth factor receptor 2 status, and were able to provide informed consent. Patients with 0 to 1 previous lines of chemotherapy for metastatic disease were eligible. Additional inclusion criteria were: Karnofsky Performance Status score $\geq$ 70%; resolution of grade $\geq$ 2 toxicity from prior therapy (other than alopecia); peripheral neuropathy grade $\leq$ 1; neutrophil count $\geq$ 1500/mm^3; platelets $\geq$ 100,000 cells/mm^3; hemoglobin $\geq$ 9.0 g/dL; and adequate hepatic and renal function. Patients were excluded if they were receiving any other investigational agents; had untreated or symptomatic central nervous system metastases; had a known allergy to paclitaxel; had received a taxane for adjuvant therapy or metastatic disease in the last 12 months; or had any serious uncontrolled infection.

Treatment Plan

Baseline evaluations included a complete medical history and physical examination. Blood was obtained for complete blood cell counts and metabolic panels. A contrast-enhanced computed tomography scan of the chest, abdomen, and pelvis was conducted prior to treatment initiation.

nab-Paclitaxel was administered on an outpatient basis at a dose of 100 mg/m^2 intravenously on days 1, 8, and 15 of a 28-day cycle. Patients were followed for adverse events throughout the study period, and these were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0.[26] Hospitalizations related to chemotherapy-related toxicity were recorded.

Drug delays were allowed for patients with grade $\geq$ 2 neutropenia, platelet count $<$ 100,000/mm^3, and hemoglobin $\leq$ 9.0g/dL. *nab*-Paclitaxel was held in cases of grade 2 to 3 peripheral neuropathy and restarted at a dose of 80 mg/m^2 after neuropathy became grade $\leq$ 1. Patients with other grade $\geq$ 3 toxicities, as well as those with grade 1 to 2 toxicities deemed significant by the treating physician, could also have a dose delay or reduction at physician discretion.

Response Assessment

Computed tomography scans of the chest, abdomen, and pelvis were performed every 2 cycles or sooner if clinically indicated.

Treatment was continued until disease progression, unacceptable toxicity, or withdrawal of consent. Responses were assessed according to the Response Evaluation Criteria in Solid Tumors (RECIST) guidelines.[27]

GA and Chemotherapy Toxicity Risk Score

A GA was completed prior to study initiation, prior to the third cycle of therapy, and at study termination. This tool[28,29] included an evaluation of functional status (Activities of Daily Living[30] and Instrumental Activities of Daily Living [IADL])[31]; physical function (Timed Up and Go test,[32] number of falls,[33] comorbidities [Older Americans Resources and Service comorbidity scale])[34]; number of medications; cognition (Blessed Orientation-Memory-Concentration test)[35]; psychological state (Mental Health Inventory-17)[30]; social support (Medical Outcomes Study Social Support survey)[30]; social functioning (Medical Outcomes Study Social Activity Limitations Measure)[30]; and nutritional status (body mass index and self-reported weight loss).

The CARG chemotherapy toxicity risk score was calculated for each patient at baseline prior to the first cycle of *nab*-paclitaxel.[18,19] The variables included in the prediction model and scoring algorithms, as well as risk of toxicity by score, are shown in Figure 1. Patients were categorized as being at low, intermediate, or high risk of chemotherapy toxicity according to their risk score.

Statistical Analysis

Rates and associated 95% confidence limits were estimated for: (1) grade $\geq$ 2 chemotherapy toxicity; (2) dose reductions, delays, and holds; (3) hospitalizations; and (4) ORR. Median PFS and OS were estimated using the method of Kaplan and Meier. Descriptive statistics for patient demographics, number of cycles received, tumor characteristics, and geriatric assessment results are provided.

The baseline chemotherapy toxicity risk (represented by the rate of chemotherapy toxicity risk) was skewed to the right, indicating a log transformation, so we used a $\log_2$ transformation in order to analyze changes based on doubling of the rate of toxicity risk. We compared the $\log_2$ toxicity risk for participants who had at least 1 dose reduction, dose hold, or hospitalization to those that did not using a 2-tailed, 2-sample Student *t* test assuming unequal variances. The Fisher's exact test was used to compare the rates of grade 3 and above toxicities across CARG toxicity risk categories, and linear regression was used to determine if the toxicity risk predicted the number of courses completed.

Results

Patient Characteristics

Forty patients (mean age, 73 years; range, 65-87 years) were enrolled between June 2012 and January 2016. Thirty-eight (95%) enrolled at City of Hope and 2 (5%) at Ohio State. Table 1 displays the baseline characteristics and geriatric assessment results of the study patients. Forty percent (n = 16) were $\geq$ 75 years of age. Most participants were female (95%; n = 38), white (73%; n = 29), and non-Hispanic (83%; n = 33). Seventy-five percent (n = 30) had hormone receptor-positive tumors. Fifty-eight percent (n = 23) received *nab*-paclitaxel as their first line of chemotherapy for metastatic disease.

Tolerability

The median number of completed cycles was 6 (range, 0-33). Seventy-five percent (n = 30; 95% confidence interval [CI], 59%-87%) had $\geq$ 1 dose hold and 50% (n = 20; 95% CI, 34%-66%) had $\geq$ 1 dose reduction. Ten percent of participants (n = 4; 95% CI, 3%-24%) experienced delays in $\geq$ 1 cycle.

Ninety percent (n = 36; 95% CI, 76%-97%) had grade 2 or above toxicities that were attributable to treatment. Fifty-eight percent (n = 23) had grade 3 or above toxicities that were attributable to treatment. Only 1 participant had a grade 4 toxic event.

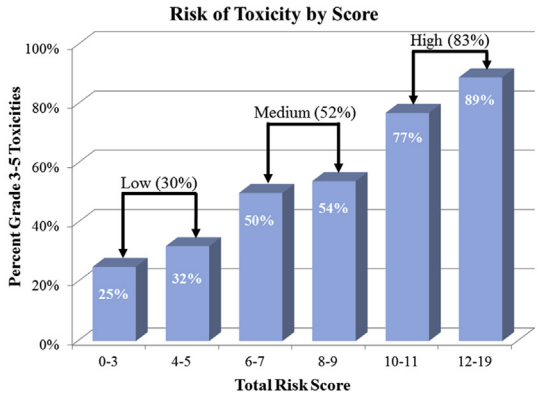
Figure 1 A, Prediction Model and Scoring Algorithm for Chemotherapy Toxicity; B, Percent Risk of Toxicity by Score

A

Variable	Value/Response	Score
Age of patient	≥ 72 years	2
	<72 years	0
Cancer type	GI or GU cancer	2
	Other cancer types	0
Planned chemotherapy dose	Standard dose	2
	Dose reduced upfront	0
Planned no. of chemotherapy drugs	Polychemotherapy	3
	Monochemotherapy	0
Hemoglobin	<11g/dL (male), <10g/dL (female)	3
	≥11g/dL (male), ≥10g/dL (female)	0
Creatinine clearance (Jeliffe ideal weight)	<34 mL/min	3
	≥34 mL/min	0
How is your hearing (with a hearing aid, if needed)?	Fair, poor, or totally deaf	2
	Excellent or good	0
No. of falls in the past 6 months	≥1	3
	None	0
Can you take your own medicine?	With some help/unable	1
	Without help	0
Does your health limit you in walking one block?	Somewhat limited/limited a lot	2
	Limited none of the time or a little of the time	0
During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?	Limited some of the time, most of the time, or all of the time	1
	Limited none of the time or a little of the time	0

See Hurria et al., *J Clin Oncol*, 2011; Abbreviation: GI, gastrointestinal; GU, genitourinary.

B



Abbreviations: GI = gastrointestinal; GU = genitourinary.

Table 1 Patient Demographic and Geriatric Assessment Results

Characteristic	Total (N = 40)	
	N	%
Age, y		
65-69	15	38
70-74	9	23
≥ 75	16	40
Gender		
Male	2	5
Female	38	95
Race		
Asian	6	15
Black	4	10
Caucasian	29	73
Other	1	3
Receptor status		
HR-positive	30	75
Triple-negative	10	25
Treatment line		
First line	23	58
Second line	17	43
IADL		
Median (range)	13	6-14
Dependence in at least 1 IADL	24	60
ADL (0-100)		
Mean (SD)	53.7	27.94
Dependence in ADL	26	65
≥ 1 fall in the previous 6 months	9	22.5
≥ 6% weight loss in the previous 6 months	10	25
Comorbidities		
Median (range)	3	0-6
Abnormal cognitive screening	3	7.5
Mental Health Inventory (0-100)		
Median (SD)	74.1	16.51
Social Support Survey (0-100)		
Mean (SD)	82.7	18.11
Hemoglobin level, g/dL		
Mean (SD)	11.8	1.61
< 11 (male), < 10 (female)	6	15
Creatinine clearance < 34 mL/min (Jeliffe)	3	7.5

Abbreviations: ADL = activities of daily living; HR = hormone receptor; IADL = instrumental activities of daily living; SD = standard deviation.

Ten percent (n = 4) experienced grade ≥ 2 peripheral sensory neuropathy (grade 2, 5%; n = 2; grade 3, 5%; n = 2). Thirty percent of the patients (n = 12; 95% CI, 17%-47%) were hospitalized owing to chemotherapy toxicity during the study period, and 28% (n = 11; 95% CI, 15%-44%) stopped treatment owing to treatment-related toxicity. Table 2 summarizes the most commonly observed adverse events.

Thirty-five percent (n = 14) of the patients were responders (95% CI, 21%-52%), with 3% (n = 1) complete response and 33% (n = 13) partial response. Forty percent (n = 16) of the patients achieved stable disease; 10% (n = 4) had disease progression; and 15% (n = 6) came off of treatment before 2 cycles. The median PFS was 6.5 months, (95% CI, 5.5 months to undefined), and the median OS was 21.2 months (95% CI, 14.6 months to undefined).

GA and Chemotherapy Risk Score

The results of the GA prior to treatment are shown in Table 1. Sixty percent (n = 24) of the patients required assistance in at least 1 IADL. Twenty-three percent (n = 9) reported at least 1 fall in the previous 6 months, 25% had involuntary weight loss, and 3% had an abnormal cognitive screening. One-half of the patients had ≥ 3 comorbidities. The mean score on the Mental Health Inventory-17 questionnaire (scores, 0-100) was 74 (SD, 16.5), and 35% (n = 14) reported poor emotional support. Using the CARG chemotherapy toxicity risk score, 53% (n = 21) of the patients were categorized at low, 38% (n = 15) at intermediate, and 10% (n = 4) at high risk of grade ≥ 3 chemotherapy toxicity (Figure 2).

Chemotherapy Risk Score and Tolerability

Because only 4 patients were in the high-risk category using the chemotherapy toxicity risk calculator, high and intermediate risk categories were combined. Patients with an intermediate or high toxicity risk had a higher risk of grade ≥ 3 chemotherapy toxicities than those with a low toxicity risk (odds ratio, 5.8; 95% CI, 1.3-33.1; $P = .01$) (Figure 2). Patients who had a dose reduction owing to chemotherapy toxicity were found to have a significantly higher mean toxicity risk than those who did not required a dose reduction (ratio of the group means = 1.38; 95% CI, 1.04-1.80; $P = .02$) (Figure 3A).

Patients who were hospitalized owing to chemotherapy toxicity had a significantly higher mean toxicity risk than those who were not hospitalized (ratio of the group means = 1.5; 95% CI, 1.13-2.00; $P < .01$) (Figure 3B). The toxicity risk was a significant predictor of the number of completed courses. A doubling in rate of toxicity risk resulted in a reduction in the number of completed courses by 4.5 (SE = 1.4; $P < .01$) (Figure 4).

Discussion

Among older adults with metastatic breast cancer receiving weekly *nab*-paclitaxel, more than one-half experienced grade 3 or higher chemotherapy toxicity. However, a GA-based risk score was able to predict treatment tolerability, and patients with higher toxicity risk were more likely to experience grade ≥ 3 toxicity, to need dose reductions, to receive fewer treatment cycles, and to be hospitalized than those with lower risk scores.

Determining the best treatment strategy for an older patient with metastatic breast cancer is a difficult task for clinicians. Therapeutic decisions are often based on chronological age alone, and older patients are less likely to receive standard, evidence-based care.[36] One reason for this is the underrepresentation of older adults (particularly those who are vulnerable and/or frail) in therapeutic clinical trials.[6] Therefore, understanding the tolerability and efficacy of chemotherapy in older adults, including those who are vulnerable and/or frail, is one of the highest priorities in geriatric oncology.[8]

This study evaluated a widely used agent, *nab*-paclitaxel, in a population of older adults with a significant proportion of

Table 2 Toxicities Experienced

Adverse Event Category	Grade 2, n (%)	Grade 3, n (%)	Grade 4, n (%)
Non-hematologic toxicities[a]	18 (45)	14 (35)	0 (0)
Heart failure	0 (0)	1 (3)	0 (0)
Diarrhea	3 (8)	3 (8)	0 (0)
Mucositis oral	0 (0)	1 (3)	0 (0)
Nausea	1 (3)	3 (8)	0 (0)
Vomiting	0 (0)	4 (10)	0 (0)
Fatigue	20 (50)	2 (5)	0 (0)
Pain	2 (5)	0 (0)	0 (0)
Allergic reaction	3 (8)	0 (0)	0 (0)
Infections and infestations other, specify	2 (5)	0 (0)	0 (0)
Upper respiratory infection	6 (15)	1 (3)	0 (0)
Urinary tract infection	4 (10)	1 (3)	0 (0)
Nail infection	2 (5)	0 (0)	0 (0)
Alanine aminotransferase increased	0 (0)	1 (3)	0 (0)
Aspartate aminotransferase increased	0 (0)	2 (5)	0 (0)
Dehydration	4 (10)	2 (5)	0 (0)
Hypocalcemia	1 (3)	1 (3)	0 (0)
Hypokalemia	2 (5)	1 (3)	0 (0)
Hyponatremia	0 (0)	1 (3)	0 (0)
Muscle weakness upper limb	0 (0)	1 (3)	0 (0)
Encephalopathy	0 (0)	1 (3)	0 (0)
Peripheral sensory neuropathy	2 (5)	2 (5)	0 (0)
Stroke	0 (0)	1 (3)	0 (0)
Cough	2 (5)	0 (0)	0 (0)
Dyspnea	2 (5)	1 (3)	0 (0)
Hypoxia	1 (3)	1 (3)	0 (0)
Hypotension	3 (8)	0 (0)	0 (0)
Thromboembolic event	1 (3)	1 (3)	0 (0)
Hematologic toxicities[a]	18 (45)	12 (30)	1 (3)
Anemia	13 (33)	7 (18)	0 (0)
Lymphocyte count decreased	6 (15)	1 (3)	0 (0)
Neutrophil count decreased	13 (33)	3 (8)	1 (3)
White blood cell decreased	21 (53)	4 (10)	0 (0)

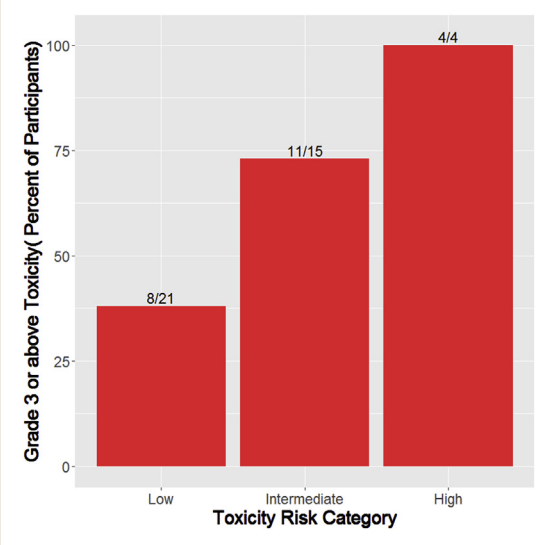
[a]Per Common Terminology Criteria for Adverse Events version 4.0; all Grade 3-4 toxicities or Grade 2 experienced by more than 1 participant.

functional deficits and comorbidities. *nab*-Paclitaxel could represent a less toxic alternative to solvent-based taxanes in vulnerable older patients owing to the lower incidence of allergic reactions and because no steroid premedication is needed.[24,25] Furthermore, we have previously demonstrated that pharmacodynamic variables of *nab*-paclitaxel are not influenced by chronological age.[37] In the randomized controlled trial (RCT) leading to approval of *nab*-paclitaxel, only 13% (n = 62) of the patients were older than 65,[38] and only 32 patients age $\geq$ 70 received *nab*-paclitaxel in a recently published RCT comparing various treatments among 799 patients with metastatic breast cancer.[39]

The proportion of patients with severe toxicity in our study was different than previously reported in a pooled analysis of patients older than 65 treated with *nab*-paclitaxel, with fewer cases of grade 3 neutropenia and sensory neuropathy in our cohort.[25] The lower incidence of neuropathy may be related to the very strict criteria for dose hold and dose reduction in our study compared with previous trials. *nab*-Paclitaxel was held in patients with grade 2 neuropathy and restarted at an 80% dose, whereas in previous trials, patients with grade 2 neuropathy have undergone dose reduction without dose holds.[39] In contrast, the ORR of 35% and the PFS of 6.5 months found in our study population were similar to those previously reported in a phase II trial utilizing a similar dosage of weekly *nab*-paclitaxel (45% and 7.5 months, respectively).[40] Of note, in that trial the mean age of the participants was 53.9 years, and only 17% were older than 65.

We have previously shown that a GA-based risk score can be used to predict severe chemotherapy toxicity in older patients across tumor types, and that the tool outperforms usual oncology assessments such as Karnofsky Performance Status.[18,19] In the present study, we evaluated the performance of our risk score to predict the tolerability of *nab*-paclitaxel in older patients with metastatic breast

Figure 2 Number of Participants With Grade 3 to 4 National Cancer Institute Common Terminology Criteria for Adverse Events by Cancer and Aging Research Group (CARG) Risk Category



cancer. Our results show that in this population, the risk score can identify patients who are at a high risk of experiencing severe toxicity or hospitalization, as well as those less likely to complete the planned treatment. Thus, this tool can potentially be integrated into RCTs in order to allocate patients to different treatment strategies, thus allowing for the enrollment of vulnerable and/or frail patients. A similar strategy was utilized in the recently published ESOGIA trial in lung cancer,[41] in which patients were assigned to different chemotherapy doses or supportive care depending on the results of a GA. This study showed that although GA-based treatment allocation for chemotherapy did not improve PFS or OS over usual care, it resulted in less all-grade toxicity (86% vs. 93%; $P = .015$), higher quality of life scores, and fewer treatment failures without compromising survival.[40,42]

This study has limitations. First, although we were able to show that the chemotherapy risk score predicted treatment tolerability, we cannot tell whether treatment modifications or dose reductions in patients with a high risk score will lead to less toxicity or different outcomes. However, this phase II trial sets the stage for RCTs comparing usual decision-making criteria (such as chronological age or simple performance status measures) to treatment allocation utilizing the chemotherapy toxicity risk score. Second, our patients were recruited at a comprehensive cancer center, and they may not be representative of patients seen in other settings. Nevertheless, it is important to emphasize that our cohort included a significant proportion of patients who had markers of vulnerability: 60% needed assistance in IADLs, 50% had 3 or more comorbidities, 40% had involuntary weight loss, and 23% had falls in the last 6 months. Third, although we were able to identify patients at higher risk of chemotherapy toxicity, we did not assess whether experiencing toxicity led to adverse functional outcomes or worse quality of life. Finally, most of our patients were non-Hispanic white, and thus the applicability of our results to other racial and ethnic groups with differing sociodemographic characteristics is limited.

Despite these limitations, our study has several strengths. It addresses a key research priority described by the Institute of Medicine, the American Society of Clinical Oncology, and the CARG by expanding the knowledge base regarding a commonly utilized chemotherapy agent in older adults with metastatic breast cancer. Furthermore, we showed that incorporating a GA and a

Figure 3 Association Between Toxicity Risk and Dose Reductions (A), and Hospitalizations (B). The Blue Dot Represents the Mean; Red Dots Represent Individual Participant Results. The Line Within the Box Represents the Median, the Upper and Lower Ends of the Boxes Represent the 25th and 75th Percentiles, and the Ends of the Whiskers Represent the Individual Result Within 1.5 Times the Interquartile Range

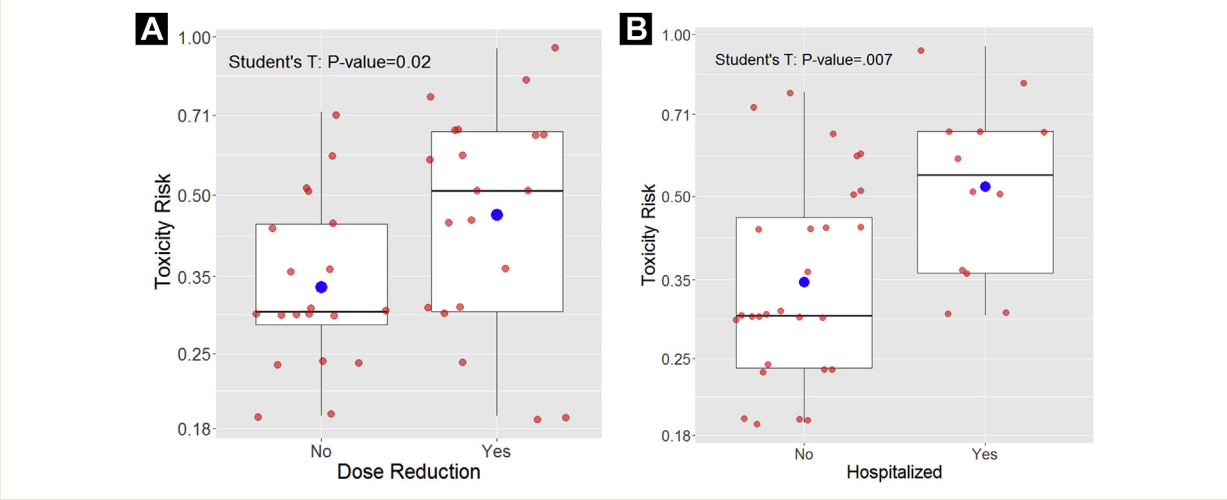
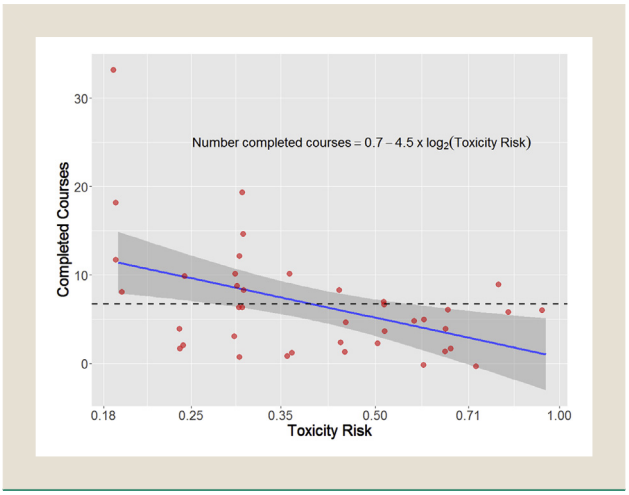


Figure 4 Association Between Toxicity Risk Score and Number of Courses Completed



chemotherapy toxicity risk score could identify patients who were less likely to tolerate treatment. This, in turn, could help clinicians and their older patients weigh the risks and benefits of treatment, ultimately personalizing cancer care.

Clinical Practice Points

- Few clinical trials exploring the use of chemotherapy in metastatic breast cancer have focused on older patients.
- *nab*-Paclitaxel may be an attractive option in older adults with metastatic breast cancer because it requires no premedication and has lower rate of hypersensitivity reactions.
- In this phase II trial, we evaluated the tolerability and efficacy of *nab*-paclitaxel among women aged 65 years and older with metastatic breast cancer.
- All patients underwent a cancer-specific GA, and a previously validated chemotherapy toxicity risk score was calculated for each patient. We explored the use of this risk score to predict chemotherapy-related toxicity, as well as the need for dose reductions, delays, and hospitalizations.
- Forty older adults were included in the study. Fifty-eight percent had grade 3 or higher toxicities, and 30% were hospitalized owing to toxicity; 35% had an objective response to treatment. The median PFS was 6.5 months, and the median OS was 21.2 months. Patients with intermediate/high toxicity risk scores had higher risk of grade ≥ 3 toxicity than those with low risk scores. A higher mean risk score was associated with higher likelihood of dose reductions and hospitalizations.
- A GA-based chemotherapy toxicity risk score could identify older patients who are less likely to tolerate treatment. This could help clinicians and their older patients weigh the risks and benefits of treatment, leading to improvements in personalized cancer care.

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Disclosure

A. Noonan declares consulting/advisory role for Helsinn Healthcare. G. Somlo declares consulting/advisory roles for Celgene, AstraZeneca, Abbvie, Pfizer, Takeda, and Puma Biotechnology; speakers' bureau for Takeda; research funding from Celgene, Roche, and Agendia. D. Li declares consulting/advisory roles for Lexicon, Novartis, and Ipsen; speakers' bureau for Lexicon. Y. Yuan declares consulting/advisory roles for Novartis and Pfizer; research funding from Eisai, Pfizer, and Merck. A. Hurria declares consulting/advisory roles for GTx, Boehringer Ingelheim, On Q Health, Sanofi, OptumHealth, Pierian Biosciences, and MJH Healthcare Holdings LLC; research funding from GSK, Celgene, and Novartis. J. Mortimer declares honoraria from Novartis; consulting/advisory roles from Puma Biotechnology, Pfizer, and Novartis. The remaining authors have stated that they have no conflicts of interest.

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