Prospective Study Testing a Simplified Paclitaxel Premedication Regimen in Patients with Early Breast Cancer

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Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Breast cancer • Dose-dense chemotherapy • Premedication • Hypersensitivity • Paclitaxel

ABSTRACT

Background. In early trials, hypersensitivity reactions (HSRs) to paclitaxel were common, thus prompting the administration of antihistamines and corticosteroids before every paclitaxel dose. We tested the safety of omitting corticosteroids after cycle 2 during the paclitaxel portion of the dose-dense (DD) doxorubicin-cyclophosphamide (AC)–paclitaxel regimen.

Patients, Materials, and Methods. In this prospective, single-arm study, patients who completed four cycles of DD-AC for stage I–III breast cancer received paclitaxel 175 mg/m^2 every 2 weeks for four cycles. Patients received a standard premedication protocol containing dexamethasone, diphenhydramine, and a histamine H2 blocker prior to the first two paclitaxel cycles. Dexamethasone was omitted in cycles three and four if there were no HSRs in previous cycles. We estimated the rate of grade 3–4 HSRs.

Results. Among 127 patients enrolled, 125 received more than one dose of protocol therapy and are included in the analysis. Fourteen (11.2%; 90% confidence interval, 6.9%–20.0%) patients had any-grade HSRs, for a total of 22 (4.5%; 3.1%–6.4%) HSRs over 486 paclitaxel cycles. Any-grade HSRs occurred in 1.6% (0.3%–5.0%), 6.5% (3.3%–11.3%), 7.4% (3.9%–12.5%), and 2.6% (0.7%–6.6%) of patients after paclitaxel cycles 1, 2, 3, and 4, respectively. Dexamethasone use was decreased by 92.8% in cycles 3 and 4. Only one patient experienced grade 3 HSR in cycles 3 or 4, for a rate of grade 3/4 HSR 0.4% (0.02%–2.0%) (1/237 paclitaxel infusions). That patient had grade 2 HSR during cycle 2, and the subsequent grade 3 event occurred despite usual dexamethasone premedication. A sensitivity analysis restricted to patients not known to have received dexamethasone in cycles 3 and 4 found that any-grade HSRs occurred in 2.7% (3/111; 0.7%–6.8%) and 0.9% (1/109; 0.05%–4.3%) of patients in cycle 3 and 4, respectively.

Conclusion. Corticosteroid premedication can be safely omitted in cycles 3 and 4 of dose-dense paclitaxel if HSRs are not observed during cycles 1 and 2. The Oncologist 2021;26:927–933

Implications for Practice: Because of the potential for hypersensitivity reactions (HSRs) to paclitaxel, corticosteroids are routinely prescribed prior to each dose, on an indefinite basis. This prospective study, including 125 patients treated with 486 paclitaxel cycles, demonstrates that corticosteroids can be safely omitted in future cycles if HSRs did not occur during cycles 1 and 2 of paclitaxel and that this strategy reduces the use of corticosteroids in cycles 3 and 4 by 92.8% relative to current standard of care.

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In early clinical trials of paclitaxel, hypersensitivity reactions (HSRs) to paclitaxel occurred in up to 30% of patients [1–4]. After the introduction of premedication with antihistamines and corticosteroids, and prolongation of infusion time, the rate of severe reactions was reduced to 2%–4% [1, 5]. Conventional practice is to administer 12–20 mg of dexamethasone (frequently as two doses starting the evening before chemotherapy), H1-receptor antagonists, and H2-receptor antagonists prior to every cycle of paclitaxel. The current packaging insert for paclitaxel contains a black box warning that all patients should be pretreated with corticosteroids, diphenhydramine, and H2-antagonists [6].

However, the majority of HSRs to paclitaxel occur within the first two cycles. In a study of 450 patients who received paclitaxel premedication, 44 (9%) patients experienced a total of 71 infusion reactions. Notably, 48% of infusion reactions occurred during the initial cycle of paclitaxel, with 23%, 13%, 8%, and 4% of reactions during cycles 2, 3, 4, and 5, respectively [2]. Of the 44 patients who experienced at least one HSR, 77% experienced a reaction during cycle 1, and 18% had their first reaction during cycle 2. Only 5% of patients experienced an initial reaction after the second cycle of paclitaxel.

Given the potential adverse events related to repeated corticosteroid administration over the course of paclitaxel chemotherapy, including the risk of hyperglycemia, steroid-related acne, agitation, insomnia, and weight gain/fluid retention and the potential association with Pneumocystis jiroveci pneumonia [7], reducing the use of corticosteroid premedication during paclitaxel could be beneficial, if feasible. Therefore, we hypothesized that a simplified, corticosteroid-sparing, premedication regimen, including omission of dexamethasone in cycles 3 and 4 for patients who did not experience HSRs during their first two cycles of paclitaxel, would be safe and feasible, and associated with an acceptably low rate of HSRs.

To test this hypothesis, we conducted a multicenter, single-arm phase II study in patients with early breast cancer receiving adjuvant dose-dense doxorubicin-cyclophosphamide (AC) followed by dose-dense paclitaxel. Although the primary study endpoint was to test the feasibility and safety of omitting routine growth factor prophylaxis with paclitaxel (and has been reported separately) [8], a study prespecified secondary endpoint was to test the safety of a simplified premedication regimen, including omission of routine corticosteroids prior to cycles 3 and 4 of paclitaxel. We report on these outcomes here.

**Patients, Materials, and Methods**

**Eligibility**
Women or men 18 to 65 years of age with stage I–III HER2-negative breast cancer for whom neoadjuvant or adjuvant dose-dense AC-paclitaxel was deemed clinically indicated by the treating oncologist were eligible for inclusion. Patients who had experienced febrile neutropenia during AC chemotherapy were excluded, as were patients who had received prior cytotoxic chemotherapy (other than immediately preceding AC) or previous therapeutic radiation in the past 5 years. No concurrent use of investigational agents was permitted.

The study was approved by the Dana-Farber/Harvard Cancer Center Institutional Review Board. All participants signed informed consent prior to initiation of any study procedures. Participating centers were Dana-Farber Cancer Institute (DFCI, Boston, MA), DFCI Milford (Milford, MA), South Shore Hospital (South Weymouth, MA), New Hampshire Oncology-Hematology (Londonderry, NH), and St. Elizabeth’s Medical Center (Boston, MA).

**Treatment Plan**
Chemotherapy could be given in either the neoadjuvant or adjuvant setting. Two weeks after the completion of four cycles of dose-dense AC chemotherapy, paclitaxel was administered at 175 mg/m² intravenously (IV) as a 3-hour infusion, once every 2 weeks for four cycles.

In order to initiate each cycle of paclitaxel, patients were required to have absolute neutrophil count (ANC) ≥10,000/μL and platelets ≥100,000/mm³. Other grade 3 or clinically significant grade 2 (with the exception of alopecia) nonhematological toxicities were required to have resolved to grade 1 before re-treatment. Paclitaxel was to be discontinued for grade ≥3 neurotoxicity. Treatment was given until unacceptable toxicity, withdrawal of consent, or other changes to the participant’s condition that would make further treatment unacceptable to either the participant or treating investigator.

Prior to receipt of the first two cycles of paclitaxel, the following premedication regimen was given: a single dose of dexamethasone 12 mg p.o. taken approximately 2–6 hours prior to infusion; diphenhydramine 25 or 50 mg p.o./IV 30–60 minutes prior to infusion; and any histamine H2 blocker (ranitidine 150 gm p.o. or 50 mg IV; famotidine 20 mg p.o./IV; or equivalent) 30–60 minutes prior to infusion. If, after completion of the first two cycles of paclitaxel, no HSRs had occurred, dexamethasone was discontinued completely. Diphenhydramine and H2 blocker premedication were maintained. If any-grade HSRs occurred during either cycle 1 or 2 of paclitaxel, dexamethasone premedication was maintained, and the premedication regimen could be further adjusted according to the discretion of the treating physician. Treatment-emergent HSRs were treated according to protocol-specified guidelines. Patients who experienced grade 4 HSRs were taken off study.

**Toxicity Assessments**
Adverse events were graded using Common Terminology Criteria for Adverse Events version 4.0. Patients were assessed at each study visit, including physical examination and review of systems. An after study safety assessment, conducted either in person or by telephone, occurred 4–8 weeks after the last dose of paclitaxel. Blood counts, including ANC, were collected centrally via review of laboratory reports. In this pragmatic trial, a simplified assessment for nonhematologic toxicity was incorporated, including only prospective collection of relevant toxicities, such as...
grade 3–4 toxicities or any toxicity that led to dose reduction/dose delay/discontinuation. Additional review of patient medical records including notes and infusion center records was conducted for all patients to ensure accuracy of all-grade HSR reporting and fidelity to the protocol-specified premedication guidelines.

Statistical Plan
The primary endpoint of this single-arm, phase II study was the on-time completion rate of four cycles of paclitaxel omitting routine use of peg–filgrastim using prespecified safety rules. The target sample size was 125 evaluable patients, in order to have adequate power to evaluate this endpoint. Results of this analysis are reported separately.

A prespecified secondary endpoint was the safety of a simplified paclitaxel premedication regimen with respect to the rate of HSRs. We aimed to estimate the rate of grade 3/4 HSRs in cycles 3 and 4 in the entire study population. As a safety stopping rule, the rate of grade 3/4 HSRs was to be evaluated after 51 patients were enrolled. If the rate of grade 3/4 HSRs in cycles 3–4 was >10%, the regimen would be considered too toxic. If 2 out of 51 patients experienced a grade 3/4 HSR in cycles 3–4, the rate of grade 3/4 is 4% (90% confidence interval [CI], 1%–12%). If 2 or more patients (of the first 51 patients) experienced a grade 3/4 HSR in cycles 3–4, the regimen would be considered too toxic and the premedication substudy would be terminated, and future patients would receive standard paclitaxel premedication. Otherwise, the simplified premedication regimen would be continued in the remainder of patients and the HSR rate estimated across the study population.

Statistical Analysis
Descriptive statistics were used to describe the patient and disease characteristics, treatment received, and adverse events. The rate of HSR was reported along with the 90% confidence interval. All analyses were performed using R version 3.2.3 (R Foundation, Vienna).

Results
Patient Characteristics
Between May 2016 and November 2018, 127 patients were registered, of whom 125 received at least one dose of paclitaxel on protocol and are included in the final analysis. Of the two unevaluable patients, one withdrew consent, and one was found ineligible after registration but prior to start of paclitaxel. Baseline characteristics are listed in Table 1. Median age was 46 years (range, 21–65). Most (81%) of the study population self-identified as White, and most (95%) had an Eastern Cooperative Oncology Group Performance Status of 0. Two thirds (67%) of patients were premenopausal. Chemotherapy was delivered in the neoadjuvant setting in 46% of participants.

Premedication and Treatment
Patients completed a total of 486 paclitaxel cycles on protocol. Among the 125 patients included in this analysis who received the first cycle of paclitaxel, 124 completed cycle 2, 122 completed cycle 3, and 115 completed cycle 4. All patients received dexamethasone during cycles 1 and 2. A total of three patients received dexamethasone during cycles 3 and/or 4 even without previous HSRs leading to study violations in a total of four cycles of paclitaxel.

Rates of Hypersensitivity Reactions
During the whole study, 14 (11.2%, 90% CI, 6.9%–20.0%) patients had any-grade HSRs. Among these, one patient had HSRs in three cycles, six had HSRs in two cycles, and seven had HSRs in a single cycle. Thus, a total of 22 (4.5%, 3.1%–6.4%) HSRs occurred following 486 cycles of paclitaxel. Any-grade HSRs occurred in 1.6% (0.3%–5.0%), 6.5% (3.3%–11.3%), 7.4% (3.9%–12.5%), and 2.6% (0.7%–6.6%) of patients after cycles 1, 2, 3, and 4 of paclitaxel, respectively. The vast majority of HSRs were grade 1 or 2; notably, there was only one grade 3 HSR event observed, for a rate of

| Table 1. Patient and disease characteristics (n = 125) |
|-----------------------------------------------|
| **Characteristic** | **No. of patients (%)** |
| Age at registration, median (range), yr | 46 (21–65) |
| Race | |
| White | 101 (81) |
| Black | 9 (7) |
| Asian | 5 (4) |
| Other | 10 (8) |
| Ethnicity | |
| Hispanic or Latino | 7 (6) |
| Non-Hispanic | 113 (90) |
| Not known | 5 (4) |
| ECOG PS at Baseline | |
| 0 | 119 (95) |
| 1 | 6 (5) |
| Menopausal status | |
| Premenopausal | 84 (67) |
| Postmenopausal | 41 (33) |
| Stage at Initial Diagnosis | |
| I | 16 (13) |
| II | 81 (65) |
| III | 27 (22) |
| Unknown | 1 (1) |
| Histology | |
| Ductal carcinoma | 94 (75) |
| Lobular carcinoma | 16 (13) |
| Mixed ductal lobular carcinoma | 13 (10) |
| Other | 2 (2) |
| Hormone receptor status | |
| ER and/or PR positive | 80 (64) |
| ER and PR negative | 44 (35) |
| Unknown | 1 (1) |
| Chemotherapy setting | |
| Neoadjuvant | 57 (46) |
| Adjuvant | 68 (54) |

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group Performance Status; ER, estrogen receptor; PR, progesterone receptor.
grade 3/4 HSRs of 0.4% (0.02%–2.0%) (1/237 paclitaxel infusions) in cycles 3 and 4 of paclitaxel. This patient had experienced a grade 2 HSR on cycle 2, and despite having received dexamethasone premedication with cycle 3, she had grade 3 HSR with this cycle. Table 2 displays the rates of all-grade HSRs for each cycle of paclitaxel and Table 3 summarizes details of HSR symptoms for each patient.

We also conducted a sensitivity analysis restricted to patients not known to have received dexamethasone in cycles 3 (n = 111) and 4 (n = 109). We found that any-grade HSRs occurred in 2.7% (n = 3; 0.7%–6.8%) and 0.9% (n = 1; 0.05%–4.3%) of patients upon cycle 3 and 4. There were no grade 3 or 4 HSRs among these patients.

**DISCUSSION**
We prospectively tested the safety of a simplified, corticosteroid-sparing, premedication regimen during the

### Table 2. HSR rates

| Cohort and cycle number | Number of paclitaxel cycles completed | Any HSR n, (%) | Grade 3/4 HSR n, (%) |
|-------------------------|---------------------------------------|----------------|---------------------|
| Intention to treat population |                                       |                |                     |
| Cycle 1                 | 125                                   | 2 (1.6, 0.3–5.0) | 0                   |
| Cycle 2                 | 124                                   | 8 (6.5, 3.3–11.3) | 0                   |
| Cycle 3                 | 122                                   | 9 (7.4, 3.9–12.5) | 1 (0.8, 0.04–3.8)   |
| Cycle 4                 | 115                                   | 3 (2.6, 0.7–6.6) | 0                   |
| Sensitivity analysis    |                                       |                |                     |
| Cycle 3                 | 111<sup>a</sup>                       | 3 (2.7, 0.7–6.8)| 0                   |
| Cycle 4                 | 109<sup>a</sup>                       | 1 (0.9, 0.05–4.3)| 0                   |

<sup>a</sup>Without dexamethasone premedication.

### Table 3. Description of HSRs for each patient

| Subject ID | Cycle of the HSR | Use of dexamethasone as premedication | Signal and symptoms | Grade |
|------------|------------------|--------------------------------------|---------------------|-------|
| 1          | 3                | No                                   | Hypertension; tachycardia. | Grade 1–2 |
| 10         | 3                | No                                   | Abdominal cramping; hypertension. | Grade 1–2 |
| 11         | 2                | Yes                                  | Abdominal pain; back pain; chest pain; flushing. | Grade 1–2 |
| 21         | 3                | Yes                                  | Flushing; redness on top of head, face, and chest. | Grade 1–2 |
| 31         | 2                | Yes                                  | Back pain; flushing; nausea. | Grade 1–2 |
| 3         | 3                | Yes                                  | Abdominal pain; back pain; chest pain; flushing. | Grade 1–2 |
| 4         | 4                | Yes                                  | Flushing; chest tightness; flushing; hypertension; nausea. | Grade 1–2 |
| 33         | 2                | Yes                                  | Back pain; flushing; SOB; tingling sensation. | Grade 1–2 |
| 3         | 3                | Yes                                  | Back pain; flushing; SOB. | Grade 1–2 |
| 36         | 2                | Yes                                  | Flushing; feeling very warm; SOB; stomach cramping. | Grade 1–2 |
| 3         | 3                | Yes                                  | Chest tightness; stomach cramping. | Grade 1–2 |
| 84         | 4                | No                                   | Ears feeling hot and red. | Grade 1–2 |
| 89         | 1                | Yes                                  | Flushing; SOB. | Grade 1–2 |
| 90         | 2                | Yes                                  | Back pain; flushing; feeling very warm; SOB. | Grade 1–2 |
| 3         | 3                | Yes                                  | Flushing; SOB. | Grade 3 |
| 92         | 2                | Yes                                  | Chest pain/tightness; hypertension; SOB; tachycardia. | Grade 1–2 |
| 96         | 2                | Yes                                  | Flushing; itchy throat tingling and lip tingling. | Grade 1–2 |
| 115        | 2                | Yes                                  | Back pain; cough; flushing. | Grade 1–2 |
| 3         | 3                | Yes                                  | Cough; flushing; headache and backache. | Grade 1–2 |
| 117        | 1                | Yes                                  | Chest tightness; flushing/hot flash. | Grade 1–2 |

All patients received as premedication famotidine 20 mg and diphenhydramine. Diphenhydramine was given in a dose of 50 mg for most patients except in individuals 21, 33, 36 (only at cycle 2), 84, 90 (only at cycle 2), and 115 (at cycle 2) who received 25 mg.

Abbreviations: HSR, hypersensitivity reaction; SOB, shortness of breath.
paclitaxel (175 mg/m² IV over 3 hours) portion of the dose-dense AC-paclitaxel regimen for stage I–III breast cancer. The simplified regimen involved the use of a single oral 12 mg dose of dexamethasone 2–6 hours prior to infusion, along with diphenhydramine and an H2-blocker 30–60 minutes prior to infusion for the first two cycles. If no HSRs occurred during the first two cycles, then dexamethasone premedication was omitted entirely in cycles 3 and 4. We found that the simplified regimen was safe and feasible and met the prespecified safety endpoint, with a rate of grade 3/4 HSRs of 0.8% (90% CI, 0.04%–3.7%) (1/122 patients) in cycles 3 and 4 of paclitaxel. The single patient who experienced a grade 3 HSR in cycle 3 had a prior grade 2 HSR during cycle 2, and despite having received dexamethasone on cycle 3, she had grade 3 HSR.

Abbreviations: HSR, hypersensitivity reaction; NS, normal saline.

| Reference                        | Study design, number of patients | Steroid schedule                                                                 | % any HSR in cycles 3 and 4 |
|----------------------------------|---------------------------------|----------------------------------------------------------------------------------|----------------------------|
| Barroso-Sousa et al. (current study) | Prospective, single cohort, n = 125 | Dexamethasone was omitted completely in cycles 3 and 4 if there were no HSRs in previous cycles. | 4.7%                       |
| Quock et al. [14]                | Prospective cohort, n = 30      | After first infusion of paclitaxel, if no HSRs, a test dose of paclitaxel, 1 mg in 20 mL of NS, was then infused IV over 1 min. If no HSRs occurred, the patient received paclitaxel without premedication. | None                       |
| Yenilmez et al. [15]             | Retrospective analysis, n = 60  | If the first two infusions of paclitaxel were tolerated with no HSRs, all premedications were discontinued for the following infusions. | 7                          |
| Parinyanitikul et al. [16]       | Retrospective analysis, n = 85  | Withholding dexamethasone premedication in patients not experiencing HSRs after two previous cycles of weekly paclitaxel administration. | 6.25                       |
| Berger et al. [17]               | Retrospective analysis, n = 234 | Patients who did not experience an infusion HSR with their first or second dose of paclitaxel and discontinued paclitaxel premedication for subsequent doses. | 0.85                       |

*The rate of grade 3/4 HSRs was 0.8% (n = 1). This patient had a grade 2 HSR on cycle 2, and despite having received dexamethasone on cycle 3, she had grade 3 HSR.

Given the potential adverse events related to repeated corticosteroid administration over the course of paclitaxel chemotherapy, other groups have also explored the safety of omitting dexamethasone [13–17] if a patient did not experience an HSR after the first two cycles. Yenilmez et al. performed a retrospective analysis among 60 patients who received different paclitaxel regimens and were treated under an early termination protocol of a standard premedication regimen containing dexamethasone, diphenhydramine, and famotidine [15]. If tolerated with no HSR occurrence, all premedications were discontinued after the first two infusions. The authors showed that 7% had an HSR in the early termination protocol. Similarly, two other groups [16, 17] performed retrospective analyses among patients receiving paclitaxel-based chemotherapy and showed that withholding dexamethasone premedication in patients not experiencing HSRs after two previous cycles of weekly paclitaxel administration was feasible and safe. Parinyanitikul et al. evaluated 85 patients on weekly paclitaxel and found a 6.25% occurrence rate in HSRs [16]. Berger et al. analyzed 234 patients (87% on weekly paclitaxel) and observed incidence of 0.85% of HSRs [17]. Quock et al. prospectively evaluated 30 patients receiving weekly paclitaxel (50–90 mg/m²/week; 205 doses) [14]. At first dose of paclitaxel, patients received the following premedications: dexamethasone, diphenhydramine, and cimetidine. If a patient did not experience an HSR, no further premedications were given in the following infusions. A total of 205 doses of weekly paclitaxel were delivered, and no HSRs were observed during either the initial weekly dosing of paclitaxel or subsequent dosing.

With an any-grade HSR rate of <10% and a grade 3/4 HSR rate less than 1% in cycles 3 and 4 of dose-dense paclitaxel, our study confirms the feasibility and safety of eliminating routine use of dexamethasone as a premedication before cycles 3 and 4 of this regimen if no prior HSRs occurred during the first two cycles of treatment (Table 4 summarizes the findings of these studies).
Strengths of our study are its prospective design, predefined rules for dexamethasone administration/omission, and relatively large number of delivered paclitaxel cycles. We note several caveats and limitations. Three patients in this study received dexamethasone during cycles 3 and/or 4 even without previous HSRs and were considered protocol violations. Even within the context of a clinical trial, with per protocol chemotherapy order sets including the protocol-specified premedications, long-established patterns of dexamethasone usage were challenging to alter, despite repetitive training of investigators, pharmacists, infusion nurses, and patients throughout the study period. However, our sensitivity analysis, restricted to patients who did not receive dexamethasone in cycles 3 and 4, also showed a very low rate of HSRs (any-grade HSRs in 2.7% [n = 3; 90% CI, 0.7%–6.8%] during cycle 3 and 0.9% [n = 1; 90% CI, 0.05%–4.3%] of patients during cycle 4; no grade 3/4 HSRs). Finally, in the setting of this non-randomized study, we did not prospectively collect patient-reported outcomes, and the study design does not allow us to quantify the impact of the simplified premedication regimen on patient experience of paclitaxel chemotherapy.

CONCLUSION
A simplified steroid premedication regimen, with a single dose of 12 mg oral dexamethasone 2–6 hours prior to infusion of cycles 1 and 2 of paclitaxel (with diphenhydramine and an H2-blocker 30–60 minutes prior to infusion), followed by omission of routine dexamethasone during cycles 3 and 4 in patients who did not experience HSRs during the first two cycles, was safe, feasible, and associated with a < 1% rate of grade 3/4 HSRs, while reducing dexamethasone use by 92.8% relative to usual standard of care. We believe our simplification of cycles 1 and 2 of paclitaxel (with diphenhydramine –6 hours prior to infusion), followed by omission of routine dexamethasone usage were challenging to alter, despite repetitive training of investigators, pharmacists, infusion nurses, and patients throughout the study period. However, our sensitivity analysis, restricted to patients who did not receive dexamethasone in cycles 3 and 4, also showed a very low rate of HSRs (any-grade HSRs in 2.7% [n = 3; 90% CI, 0.7%–6.8%] during cycle 3 and 0.9% [n = 1; 90% CI, 0.05%–4.3%] of patients during cycle 4; no grade 3/4 HSRs). Finally, in the setting of this non-randomized study, we did not prospectively collect patient-reported outcomes, and the study design does not allow us to quantify the impact of the simplified premedication regimen on patient experience of paclitaxel chemotherapy.

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For Further Reading:
Hannah C. Timmins, Tiffany Li, Terry Trinh et al. Weekly Paclitaxel-Induced Neurotoxicity in Breast Cancer: Outcomes and Dose Response. The Oncologist 2021;26:366–374.

Implications for Practice:
Weekly paclitaxel schedules are extensively used in breast cancer. Patients may develop symptomatic and objective neuropathy early in the treatment course, with these individuals requiring closer monitoring. Furthermore, neuropathy is a long-term sequela that may impact quality of life and require appropriate supportive services. Results suggest that dose reduction does not necessarily lead to better neuropathy outcomes. Understanding schedule-specific toxicity and risk factors for neuropathy will be critical to determining individualized treatment strategies and improving quality of life in breast cancer survivors.