



Incidence of infusion hypersensitivity reaction after withholding dexamethasone premedication in early breast cancer patients not experiencing two previous cycles of infusion hypersensitivity reaction for weekly paclitaxel chemotherapy

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Abstract

Background Premedication with dexamethasone is an essential part of the prevention of hypersensitivity reaction (HSR) associated with taxane administration. However, the possibility of stopping dexamethasone premedication has been investigated in previous studies to reduce the steroid's adverse events; however, either the result or the particular protocol was limited. Thus, our study aimed to evaluate the incidence of HSR after dexamethasone premedication discontinuation after lack of HSR in two previous weekly paclitaxel infusions.

Method Early breast cancer patients who received adjuvant weekly paclitaxel in a retrospective cohort from January 2012 through February 2016 at the King Chulalongkorn Memorial Hospital were reviewed. All patients received a standard premedication protocol prior to the first and second paclitaxel infusion. Dexamethasone was omitted in later cycles in all patients who did not undergo infusion HSR. Patients who developed HSR during the first or second cycles of paclitaxel infusion were excluded. The incidence of HSR during the later cycle of paclitaxel administration and factors associated with this adverse reaction were collected.

Results Eighty-one of 85 patients who did not undergo infusion HSR after 2 cycles of weekly paclitaxel administration were retrospectively reviewed. The median age was 51 years (range 27–74 years). Only 16% of the patients had a BMI greater than 30 kg/m², 57.8% were premenopausal, 67.9% had no comorbidity, none had a history of allergy or asthma, 65.4% received weekly paclitaxel as a single agent, and 34.6% received weekly paclitaxel in combination with trastuzumab. Five of 81 patients reported grade I–II HSR (6.25%), which occurred mostly during the first 6 cycles (60%). Temporary discontinuation of paclitaxel infusion was observed in all HSR patients. No differences regarding age, BMI, menopausal status, and underlying disease between the HSR and no HSR groups were identified. Concerning the safety profile, peripheral neuropathy (gr I 60%, gr II 13.5%, and gr III 2.4%), myalgia (43.4%), and edema (10.5%) were commonly reported, whereas dyspepsia (5.3%) and insomnia (14.5%) were rarely described in withholding patients.

Conclusion Withholding dexamethasone premedication in non-experiencing HSR patients after two previous cycles of weekly paclitaxel administration was safe and did not impact the higher incidence of HSR. A discontinuing dexamethasone protocol should be recommended generally in these patients, especially those with a high risk for steroid-induced side effects.

Keywords Dexamethasone premedication · Paclitaxel · Infusion hypersensitivity reaction

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Introduction

Premedication, with dexamethasone plus histamine-1 and histamine-2 antagonist, is a crucial part of the prevention of hypersensitivity reaction (HSR) associated with taxane administration [1–8]. Although cremophor EL has been documented to be one of the important mechanisms of the

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paclitaxel hypersensitivity reaction, the exact mechanism is uncertain [9–11]. With standard and/or modified prophylaxis premedication, the incidence of HSR has declined from 40 to 1–2% [12].

According to the risk factors of HSR, Sendo and his colleagues reported the incidence of HSR and associated factors in 105 ovarian cancer patients who received 3 weeks of adjuvant carboplatin and paclitaxel. The incidence of HSR was 13.3% for moderate to severe grading. Several factors such as previous rash from paclitaxel, respiratory problem, obesity (body mass index >25 kg/m²), postmenopausal status, and oophorectomy were associated with both carboplatin and paclitaxel HSR [13]. Similarly, Piovano et al. [14] studied 157 ovarian cancer patients who received combination platinum and paclitaxel and reported that the significant risk factor associated with HSR was allergic history (OR 3.42, CI 0.94–12.45, $p=0.06$). Although numerous risk factors such as menopausal status, high body mass index (BMI), and history of allergy or asthma have been demonstrated and might play a role in evolving paclitaxel HSR, no strong risk factors have been reported to play essential roles in the paclitaxel hypersensitivity reaction.

Concerning the pioneering study by Quock and colleagues of weekly paclitaxel administration in 30 patients with early breast cancers who received weekly paclitaxel 50–90 mg/m², no hypersensitivity reaction was reported in patients who omitted premedication after not experiencing a previous HSR [15]. Additionally, Breaverman et al. reported that reducing the oral dose of steroid in subsequent treatments until zero was feasible without increasing HSR [16]. Moreover, Green et al. studied 302 early breast cancer patients who received weekly paclitaxel and reported that after reducing the dose of dexamethasone during the fourth cycle until the twelfth cycle in patients, who did not have a previous HSR, the incidence of grade I–III HSR was 2.3% and that of grade IV HSR was 0.3% [17]. The recently published study from Michael J Berger and his colleagues evaluated 234 breast cancer patients whose dexamethasone premedication was discontinued after none experienced HSR in the first two doses of paclitaxel-based chemotherapy [18, 19]. They showed that most of the patients did not report an infusion reaction; however, only two patients required rescue medication.

Recently, our retrospective study in Thai early breast cancer patients who received weekly paclitaxel in KCMH reported that six of the 86 patients who received weekly paclitaxel chemotherapy had grade II–III HSR (7.0%), which occurred mostly during the first 6 cycles (5/6, 83.3%). In all 984 cycles, dexamethasone was omitted in 617 subsequent cycles (62.7%). The incidence of HSR was 5/617 (0.81%) cycles without dexamethasone premedication and 3/367 (0.82%) cycles with dexamethasone premedication. There was no statistically significant difference in HSR between the

cycles that received or did not receive dexamethasone premedication ($p=0.99$) [20]. Although our retrospective study has several limitations, withholding premedication with dexamethasone in patients who do not experience hypersensitivity reactions during the first few weeks of weekly paclitaxel administration is feasible and appears to yield a similar incidence of HSR.

Even with standard premedication, HSR grades I–II and grades III–IV still developed at rates of 40 and 2–4%, respectively, for every 3 weeks of paclitaxel administration. Additionally, with the recent use of weekly paclitaxel administration in adjuvant breast cancer, HSR grade III or higher was similarly reported at a rate of less than 3%. During weekly paclitaxel administration, patients may be exposed to a high and prolonged dose of dexamethasone prophylaxis that may cause significant adverse effects such as weight gain, insomnia, and hyperglycemia. Therefore, reducing or withholding the dexamethasone premedication in patients not experiencing a previous infusion HSR was widely investigated with the safety outcomes. Withholding dexamethasone is also feasible in Thai women, but we have not had any documented information about this premedication strategy. Thus, our study was aimed to evaluate the incidence of infusion HSR after discontinuing dexamethasone premedication in patients who did not have two previous cycles of weekly paclitaxel associated with infusion HSR.

Patients and methods

Patients

Patients with early breast cancer who received adjuvant or neoadjuvant weekly paclitaxel as a single agent or in combination with trastuzumab from January 2012 through April 2016 at the King Chulalongkorn Memorial Hospital were retrospectively reviewed. Patients who received at least 6 cycles of weekly paclitaxel administration were also included in our study. Patients receiving daily doses of systemic corticosteroid for any reason, patients receiving three weekly paclitaxel administrations and patients receiving albumin-bound paclitaxel or docetaxel or concomitant corticosteroid from any disease, and patients who had disease progression before completing the study were excluded. Additionally, patients who had a history of HSR associated with taxane exposure were excluded from our study.

Treatment

All patients received the standard dose of adjuvant or neoadjuvant weekly paclitaxel, 80 mg/m². In some patients who received combination therapy with trastuzumab, the standard

loading dose of 4 and then 2 mg/m² during weekly paclitaxel was recommended. All patients underwent the standard premedication protocol prior to the first and second doses of paclitaxel infusion. The standard premedication protocol included dexamethasone 5 mg iv, diphenhydramine 25 mg iv, and ranitidine 50 mg iv administered at least 30 min prior to the start of paclitaxel administration. Dexamethasone had been omitted in later cycles in patients not experiencing two previous infusion hypersensitivity reactions. Patients who developed HSR during the first or second cycles of paclitaxel infusion were excluded.

Study endpoints

The primary endpoint was the incidence of HSR during doses three to 12 of weekly paclitaxel chemotherapy in patients who did not have two previous cycles of infusion HSR. Secondary endpoints were the associated factors with HSR and adverse reactions (AEs) from paclitaxel and dexamethasone.

Statistical analysis

Based on our previous retrospective study, the incidence rate of HSR from weekly paclitaxel was 7%, and 4.5% of the HSR patients developed during the third and later cycles. Therefore, the needed sample size in this study was approximately 100 patients for detecting HSR. The incidence of HSR was collected after reviewing medical records and nurse record forms. Patients who received additional doses of H1 antagonists (diphenhydramine or chlorpheniramine) or H2 antagonists (ranitidine) or dexamethasone or epinephrine during the third to twelfth cycles of weekly paclitaxel infusion were also defined as HSR. Among a total of 85 patients, 4 who developed HSR within 2 cycles were excluded from our study. Baseline characteristics and details of the premedication protocol, including the dose and schedule of dexamethasone, were recorded. Categorical patient and clinical features were reported using frequencies and percentages, whereas age and weight were reported using means and standard deviation. Patients were categorized into one of two groups according to their HSR: HSR and no HSR. Patient characteristics, including age, weight, BMI, menopausal status, comorbidity, and type of paclitaxel infusion, were tabulated and compared between the groups using the unpaired *t* test and exact probability test. A value of *p* value < 0.05 was considered to be significant. All statistical analyses were performed with IBM SPSS Statistics for Windows, version 22.0. (IBM Corp, Armonk, NY, US).

Results

From January 2012 to April 2016, 85 early breast cancer patients who received adjuvant or neoadjuvant weekly paclitaxel

as a single agent or in combination with trastuzumab at the King Chulalongkorn Memorial Hospital were retrospectively reviewed. Eighty-one patients who did not have two previous cycles of infusion hypersensitivity reaction were enrolled in our study. The median age was 51 years (range 27–74). The average BMI was 24.5 ± 4.78 kg/m². Only 16% of the patients in our study had a BMI greater than 30 kg/m². Approximately 57.8% were premenopausal. About 32.1% reported any comorbidity; however, none had a history of allergy or asthma. Almost 89% received paclitaxel as adjuvant chemotherapy, and approximately 65.4% received weekly paclitaxel as a single agent, while 34.6% received weekly paclitaxel in combination with trastuzumab administration. Other baseline characteristics are listed in Table 1.

Almost all but approximately 93.8% of the patients received all 12 cycles of paclitaxel. Still, two women did not complete all 12 cycles, and paclitaxel was administered for more than 6 cycles. Furthermore, omitting infusion before 12 cycles was also observed in two patients with severe paclitaxel toxicities. Discontinuing infusion was also reported in one patient who developed atrial fibrillation and heart failure during paclitaxel administration. Adding carboplatin to the usual regimen was identified in one patient who had loco-

Table 1 Patient and tumor baseline characteristics

Baseline characteristics	Breast cancer patients (<i>n</i> = 81)
Age (year) (mean ± SD)	51.0 ± 11 (range 27–74)
Body weight (kg) (mean ± SD)	59.7 ± 11.4
BMI (kg/m ²) (mean ± SD)	24.5 ± 4.78
Menopausal status	
Premenopausal	46 (57.8%)
Postmenopausal	35 (42.2%)
Comorbidity	
No	55 (67.9%)
Yes	26 (32.1%)
History of allergy or asthma	0 (0%)
Adjuvant chemotherapy regimen (number; %)	
Paclitaxel	53 (65.4%)
Paclitaxel + trastuzumab	28 (34.6%)
Pathology (number; %)	
Invasive ductal carcinoma (IDC)	79 (97.5%)
Non-invasive ductal carcinoma	2 (2.5%)
Grading (number; %)	
Grade I	4 (4.9%)
Grade II	46 (56.7%)
Grade III	31 (38.4%)
Staging (number; %)	
Stage I	2 (2.6%)
Stage II	16 (19.7%)
Stage III	63 (77.7%)

regional disease progression during neoadjuvant paclitaxel infusion. All patients received dexamethasone premedication in the early 2 cycles, and then discontinuation in later cycles was described, which followed the study's standard protocol. Two patients with no experience of HSR received dexamethasone infusion in a later cycle due to edema and skin rashes, which may be from paclitaxel adverse events.

In terms of the primary outcome, five of 81 patients reported grade I–II HSR (6.25%), which occurred mostly during the third to sixth cycles (60%). Forty percent of HSR patients received paclitaxel in combination with trastuzumab. No patient had continuously developed HSR in a later cycle. The total mean cumulative doses of dexamethasone for the HSR and no HSR groups were 36 and 11 mg, respectively. Furthermore, no difference was observed in the baseline characteristics such as age, BMI, menopausal status, comorbidity, infusion with paclitaxel alone, or combination with trastuzumab, between patients in the HSR and no HSR groups. The baseline characteristics of patients in both the HSR and no HSR groups are shown in Table 2.

Temporary discontinuation of paclitaxel infusion was observed in all HSR patients. Additionally, all women were successfully re-treated with paclitaxel in later cycles without further HSR. All essential information from the five HSR women is shown in Table 3.

In terms of adverse reactions from paclitaxel other than hypersensitivity reaction, peripheral neuropathy, myalgia, skin rash, itching, and edema were the most commonly

reported side effects. Compared with the no HSR group, a higher incidence of peripheral neuropathy grades I–II (100 vs 73.7% in HSR and no HSR), myalgia (60 vs 43.4% in HSR and no HSR), and skin rash (20 vs 7.9% in HSR and no HSR) was observed, respectively. Conversely, a higher incidence of itching (7.9 vs 0%) and edema (10.5 vs 0%) was identified between the no HSR and the HSR groups. Other adverse reactions are shown in Table 4.

Concerning adverse reactions from dexamethasone, only dyspepsia and insomnia were described in our study. Additionally, dyspepsia and insomnia were rarely described in the withholding patients (5.3 and 14.5%, respectively). The incidence of dyspepsia was higher in the no HSR group than in the HSR group (5.3 vs 0%, respectively), while a higher incidence of insomnia was identified in the HSR group than in the no HSR group (60 vs 14.5%). Other adverse reactions are shown in Table 5.

Discussion

The incidence of HSR in patients who omitted dexamethasone premedication after not experiencing HSR in the first 2 cycles was 6.25% (5 of 81 patients). Grade I–II HSR occurred mostly during the first 6 cycles (60%), and successful paclitaxel challenge was observed in all HSR patients. According to the associated factors, no differences regarding age, BMI, menopausal status, and underlying disease between the HSR and

Table 2 Patient characteristics based on the incidence of no HSR vs HSR

Patients characteristic	Total (<i>n</i> = 81)	No HSR group (<i>n</i> = 76)	HSR group (<i>n</i> = 5)	<i>P</i> value (95% CI)
Age (years; mean ± SD)	51.0 ± 11 (range 27–74)	50.7 ± 10.6 (range 27–74)	48.8 ± 10.7 (range 36–65)	0.699 [†] (− 7.85 to − 11.65)
Body weight (kg; mean ± SD)	58.7 ± 11 (range 36.3–88)	58.5 ± 11 (range 36.3–87.9)	61.2 ± 16 (range 46.2–88)	0.606 [†] (− 13.09 to 7.69)
BMI (kg/m ² ; mean)	24.5 ± 11 (range 16.3–37)	24.4 ± 4.72 (range 16.3–37)	25.0 ± 6.15 (range 19.7–35)	0.787 [†] (− 5.01 to 3.81)
BMI				
< 25 (kg/m ² ; mean)	51	47 (61.8%)	4 (80.0%)	0.655 ^{††}
25–30 (kg/m ² ; mean)	17	17 (22.4%)	0 (0.0%)	
> 30 (kg/m ² ; mean)	13	12 (15.8%)	1 (20.0%)	
Menopausal status				0.629 ^{††}
Premenopausal	46	43 (56.6%)	3 (60.0%)	
Postmenopausal	35	33 (43.4%)	2 (40.0%)	
Comorbidity				0.482 ^{††}
No	56	51 (67.1%)	4 (80.0%)	
Yes	26	25 (32.9%)	1 (20.0%)	
Adjuvant chemotherapy regimen (number; %)				0.568 ^{††}
Paclitaxel	53	50 (65.8%)	3 (60.0%)	
Paclitaxel + trastuzumab	28	26 (34.2%)	2 (40.0%)	

CI confidence interval

[†] *p* value from unpaired *t* test

^{††} *p* value from exact probability test

Table 3 Hypersensitivity reaction in five patients who did not experience two previous cycles of infusion HSR

Age (years)	Menopausal status	Underlying disease	Paclitaxel cycle in which HSR developed (cycle)	HSR grading by NCITAC version 3.0	Signs and symptoms of HSR	Note
36	Premenopausal	HTN	5th	I	Flushing	Hold 30 min, and then re-challenge without HSR. Thus, she received dexamethasone 5 mg in the 6th cycle and dexamethasone 5 mg in the 9th cycle until the last cycle, with no further HSR.
45	Premenopausal	None	8th	II	Flushing chest discomfort	She developed HSR at cycle 8. Hold 30 min, and then re-challenge without HSR, and no dexamethasone until the last cycle.
46	Premenopausal	None	3rd	II	Chest discomfort	She developed mild S/S at cycle 3 but did not notify the nurse. During cycles 4–12, she received dexamethasone 5 mg without HSR.
52	Postmenopausal	None	4th	I	Flushing	She developed HSR at cycle 4 and then received dexamethasone in a later cycle without HSR.
65	Postmenopausal	HTN DLP prolapsed uterus	9th	I	Flushing	She developed HSR at cycle 9 and then received dexamethasone in a later cycle without HSR.

Table 4 Adverse reactions of paclitaxel between the no HSR and the HSR groups

Adverse reactions	No HSR group (N = 76)	HSR group (N = 5)
Peripheral neuropathy		
Grade I	40 (60.5%)	4 (80%)
Grade II	10 (13.2%)	1 (20%)
Grade III	2 (2.6%)	0 (0%)
Myalgia		
No	43 (56.6%)	2 (40%)
Yes	33 (43.4%)	3 (60%)
Skin rash		
No	70 (92.1%)	4 (80%)
Yes	6 (7.9%)	1 (20%)
Itching		
No	70 (92.1%)	5 (100%)
Yes	6 (7.9%)	0 (0%)
Edema		
No	68 (89.5%)	5 (100%)
Yes	8 (10.5%)	0 (0%)

the no HSR groups were described. Concerning adverse reactions from paclitaxel and dexamethasone, peripheral neuropathy (gr I 60%, gr II 13.5%, gr III 2.4%), myalgia (43.4%), and edema (10.5%) were commonly reported whereas dyspepsia (5.3%) and insomnia (14.5%) were rarely described in withholding patients.

Several previous studies reported the incidence of HSR from paclitaxel in both weekly and three weekly schedules; however, most of them included a heterogeneous population, various primary tumors, various staging, and various combination chemotherapies [12–21]. Conversely, our study enrolled only early breast cancer patients who received 12 cycles of weekly paclitaxel alone and/or in combination with trastuzumab. Hence, our results strongly confirmed the feasibility of withholding the protocol in this group of patients but could not be applied in all patient populations. Moreover, to our knowledge, this is the first study about withholding dexamethasone premedication in early breast cancer patients not experiencing two previous cycles of HSR in the Asian

Table 5 Adverse reactions of dexamethasone between the no HSR and the HSR groups

Adverse reactions	No HSR group (N = 76)	HSR group (N = 5)
Dyspepsia	4 (5.3%)	0
Insomnia	11 (14.5%)	3 (60%)
Mood disturbance	0	0
Weight gain	0	0

population. Therefore, these helpful results would apply to other Asian women with breast cancer.

According to the dexamethasone premedication protocol, different strategies such as tapering or omitting dexamethasone infusion have been investigated in various studies. The first small study from Quock and his colleagues reported that no further HSR developed after omitting dexamethasone premedication in early breast cancer patients not experiencing HSR [15]. In Quock's study, dexamethasone premedication was omitted in the second cycle if no HSR was reported in the first cycle. Second, a large study from Green and colleagues in 302 early breast cancer patients who received weekly paclitaxel reported 2.3% of the HSR grades I–III and only 0.3% of the severe grade [17]. In contrast to Quock's study, dexamethasone was tapered from 10 to 4 mg if no HSR developed in cycles 4–12 [15]. Additionally, a study from Koppler H et al. reported that reducing dexamethasone to 10 mg IV prior to paclitaxel infusion was feasible and safe in 132 various cancer patients, including breast and ovarian cancer patients treated with a three weekly and/or a weekly schedule [22]. Recently, Berger and his colleagues evaluated 234 breast cancer patients whose dexamethasone premedication was discontinued after none experienced HSR in the first two doses of paclitaxel-based chemotherapy [18, 19]. The authors demonstrated that most of the patients did not report an infusion reaction, but only two patients required rescue medication. This large prospective study confirmed that the discontinuation of paclitaxel premedication in patients who did not experience a previous infusion HSR was not correlated with an increased incidence of HSR. Likewise, our small study similarly reported the low incidence of grade I–II HSR (6.25%). These two prospective studies confirmed that the discontinuation of paclitaxel premedication in breast cancer patients who did not experience a previous infusion HSR was not correlated with an increased incidence of HSR. Unlike Berger's study, our study not only included only early breast cancer patients but also those who were differently administered with a lower dose of dexamethasone premedication established from the experience in our previous retrospective study. As a result, our protocol endorses the feasibility of low-dose dexamethasone infusion, which could avoid steroid-induced toxicity.

Concerning the factors associated with HSR from paclitaxel infusion, two previous studies from Dr. Sendo [13] and Dr. Kwon [23] found that the lack of estrogen condition, a high body mass index (BMI), and a history of allergy or asthma might be involved in the increased incidence of HSR. The authors concluded that the marked depletion of estrogen may be related to a change in the sensitivity to paclitaxel by affecting vascular endothelial function and leading to the enhancement of HSR to paclitaxel. Unlike these two studies, no associated factors regarding age, menopausal status, BMI, and underlying disease had been reported in our study. With

inconsistent results, a large prospective cohort study is necessary to answer the important role of the estrogen level and risk of paclitaxel HSR.

Additionally, the long-term use of dexamethasone may have several negative impacts, such as cushingoid appearances, weight gain, hyperglycemia, hypertension, acne, dyspepsia, edema, anxiety, insomnia, depression, and infection. Reducing, tapering, or withholding dexamethasone premedication strategies may minimize the adverse effects of steroid use. Insomnia and dyspepsia were rarely described in our withholding patients. In particular, a higher incidence of insomnia was identified in the non-withholding group compared with the withholding group (60 vs 14.5%). Furthermore, recent preclinical studies also reported that dexamethasone rendered cancer cells resistant to paclitaxel infusion. Therefore, withholding the dexamethasone protocol should be extensively recommended not only in patients at high risk for steroid-induced side effects but also in patients in whom excellent outcomes are a priority.

Our retrospective study has some limitations. First, although we included only women with early breast cancer who received more than 6 cycles of weekly paclitaxel chemotherapy, the number of women in this study is relatively small, which might have affected the incidence rate of hypersensitivity reactions. Second, we included only early breast cancer patients. Thus, this withholding strategy could not be broadly recommended for the entire cancer population. Third, the majority of our patients were relatively thin population, which might not apply to other obese population. Finally, although our study was exclusively interested in adverse events from paclitaxel and dexamethasone, not all AEs were recognized. Thus, an additional well-designed cohort will help achieve the robust advantage of the withholding protocol in minimizing steroid toxicities.

Conclusion

Discontinuing dexamethasone premedication in patients who did not experience two previous HSRs is reasonable and safe. This premedication strategy should be applied in all early breast cancer patients who receive weekly paclitaxel administration, especially in patients who easily develop steroid-induced side effects.

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Compliance with ethical standards

The institutional review board of King Chulalongkorn Memorial Hospital and Chulalongkorn University approved the retrospective study.

References

- Eisenhauer EA, ten Bokkel Huinink WW, Swenerton KD, Gianni L, Myles J, van der Burg ME, Kerr I, Vermorken JB, Buser K, Colombo N (1994) European-Canadian randomized trial of paclitaxel in relapsed ovarian cancer: high dose versus low dose and long versus short infusion. *J Clin Oncol* 12(12):2654–2666. <https://doi.org/10.1200/JCO.1994.12.12.2654>
- McGuire WP et al (1996) Cyclophosphamide and cisplatin compared with paclitaxel and cisplatin in patient with stage III and IV ovarian cancer. *N Engl J Med* 344(1):1–6
- Kosmidis P, Mylonakis N, Nicolaides C, Kalophonos C, Samantas E, Boukovinas J, Fountzilas G, Skarlos D, Economopoulos T, Tsavdaridis D, Papakostas P, Bacoyiannis C, Dimopoulos M (2002) Paclitaxel plus carboplatin versus gemcitabine plus paclitaxel in non-small cell lung cancer: a phase III randomized trial. *J Clin Oncol* 20(17):3578–3585. <https://doi.org/10.1200/JCO.2002.12.112>
- Markman M, Kennedy A, Webster K, Peterson G, Kulp B, Belinson J (1997) Simplified regimen for the prevention of paclitaxel-associated hypersensitivity reaction. *J Clin Oncol* 15(12):3517. <https://doi.org/10.1200/JCO.1997.15.12.3517>
- Bookman MA, McGuire WP 3rd, Kilpatrick D, Keenan E, Hogan WM, Johnson SW, O'Dwyer P, Rowinsky E, Gallion HH, Ozols RF (1996) Carboplatin and paclitaxel in ovarian cancer: a phase I study of Gynecologic Oncology Group. *J Clin Oncol* 14(6):1895–1902. <https://doi.org/10.1200/JCO.1996.14.6.1895>
- Micha JP, Rettenmaier MA, Dillman R, Fraser P, Birk C, Brown JV (1998) Single-dose dexamethasone paclitaxel premedication. *Gynecol Oncol* 69(2):122–124. <https://doi.org/10.1006/gyno.1998.4993>
- Markman M, Kennedy A, Webster K, Kulp B, Peterson G, Belinson J (2000) Paclitaxel-associated hypersensitivity reaction: experience of the gynecologic oncology program of the Cleveland Clinic Cancer Center. *J Clin Oncol* 18(1):102–105. <https://doi.org/10.1200/JCO.2000.18.1.102>
- Van Zuylen L et al (2001) Role of formulation vehicles in taxanepharmacology. *Invest N drugs* 19(2):125–141. <https://doi.org/10.1023/A:1010618632738>
- Lassus M et al (1985) Allergic reaction associated with cremophor E containing antineoplastic. *Proc Am Clin Oncol* 4:268
- Van Zuylen L et al (2000) Inter-relationships of paclitaxel disposition, infusion duration and cremophor EL kinetics in cancer patients. *Anti-Cancer Drugs* 11(5):331–337. <https://doi.org/10.1097/00001813-200006000-00003>
- Szebeni J et al (2001) Formation of complement activating particle in aqueous solution of Taxol: possible role in hypersensitivity reaction. *Int Immuno Pharmacol* 1:712–735
- Weiss RB, Donehower RC, Wiernik PH, Ohnuma T, Gralla RJ, Trump DL, Baker JR Jr, van Echo DA, von Hoff DD, Leyland-Jones B (1990) Hypersensitivity reactions from taxol. *J Clin Oncol* 8(7):1263–1268. <https://doi.org/10.1200/JCO.1990.8.7.1263>
- Sendo T, Sakai N, Itoh Y, Ikesue H, Kobayashi H, Hirakawa T, Nakano H, Oishi R (2005) Incidence and risk factors for paclitaxel hypersensitivity during ovarian cancer chemotherapy. *Cancer Chemo and Pharma* 56(1):91–96. <https://doi.org/10.1007/s00280-004-0924-9>
- Piovano E, Pivetta E, Modaffari P, Martra F, Baima Poma C, Perotto S, Tripodi E, Zanfagnin V, Zola P, Ferrero A (2012) A search for predictive factors for hypersensitivity reactions to paclitaxel and platinum salts in chemotherapy for gynecologic pelvic neoplasm. *Gyneco and Obstetric Invest* 74(1):21–27. <https://doi.org/10.1159/000336772>
- Quock J, Dea G, Tanaka M, Gandara D, Lara P, Lau D (2002) Premedication strategy for weekly paclitaxel. *Cancer Investig* 20(5-6):666–672. <https://doi.org/10.1081/CNV-120003535>
- Braverman AS, Rao S, Salvatti ME, Adamson B, McManus M, Pierre S (2005) Tapering and discontinuation of glucocorticoid prophylaxis during prolonged weekly to biweekly paclitaxel administration. *Chemotherapy* 51(2-3):116–119. <https://doi.org/10.1159/000085618>
- GreenMC et al (2009) Rates of adverse events with low-dose dexamethasone (Dex) as premedication of weekly paclitaxel (Pac) utilized as adjuvant/neoadjuvant therapy for operable breast cancer. In Program and Abstracts of the American Society of Clinical Oncology 2009 Breast Cancer Symposium:Abstract 307
- Berger MJ, Vargo C, Vincent M, Shaver K, Phillips G, Layman R, Macrae E, Mrozek E, Ramaswamy B, Wesolowski R, Shapiro CL, Lustberg MB (2015) Stop paclitaxel premedication after two doses in patients not experiencing a previous infusion hypersensitivity reaction. *Support Care Cancer* 23(7):2019–2024. <https://doi.org/10.1007/s00520-014-2556-x>
- Berger MJ, Dunlea LJ, Rettig AE, Lustberg MB, Phillips GS, Shapiro CL (2012) Feasibility of stopping paclitaxel premedication after two dose in patients not experiencing a previous infusion hypersensitivity reaction. *Support Care Cancer* 20(9):1991–1997. <https://doi.org/10.1007/s00520-011-1303-9>
- Walailuk T et al (2016) Feasibility of withholding dexamethasone premedication in weekly paclitaxel administration and its associated adverse reactions. *Asian Biomed* 4:371–377. <https://doi.org/10.5372/1905-7415.1004.500>
- Lal LS, Gerber DL, Lau J, Dana W (2009) Retrospective evaluation of weekly paclitaxel hypersensitivity reactions reported utilizing an electronic medical record system at a tertiary cancer center. *Support Care Cancer* 17(10):1311–1315. <https://doi.org/10.1007/s00520-009-0588-4>
- Koppler H et al (2001) Dose reduction of steroid premedication for paclitaxel: no increase of hypersensitivity reactions. *Onkologie* 24(3):283–285. <https://doi.org/10.1159/000055093>
- Kwon JS, Elit L, Finn M, Hirte H, Mazurka J, Moens F, Trim K (2002) A comparison of two prophylactic regimen for hypersensitivity reaction to paclitaxel. *Gynecol Oncol* 84(3):420–425. <https://doi.org/10.1006/gyno.2001.6546>