Published in final edited form as:

Clin Genitourin Cancer. 2017 June ; 15(3): e429–e435. doi:10.1016/j.clgc.2016.12.003.

Safety of Same-Day Pegfilgrastim Administration in Metastatic Castration-Resistant Prostate Cancer Treated With Cabazitaxel With Or Without Carboplatin

Mehmet Asim Bilen¹, Diana H. Cauley², Bradley J. Atkinson², Hsiang-Chun Chen³, Diana H. Kaya⁴, Xuemei Wang³, Raghu Vikram⁴, Shi-Ming Tu², Paul G. Corn², and Jeri Kim²

¹Department of Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA, USA

²Department of Genitourinary Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA

³Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA

⁴Department of Radiology, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA

Abstract

Introduction—Although myeloid growth factors are commonly used to treat metastatic castration-resistant prostate cancer (mCRPC), the optimal timing of administration has not been well studied. We assessed the effects of same-day pegfilgrastim, a neutrophil stimulator, after cabazitaxel treatment with or without carboplatin in patients with mCRPC. We also evaluated the frequency of urinary tract inflammation during treatment.

Patients and Methods—Between September 2010 and September 2014, 151 consecutive patients with mCRPC underwent cabazitaxel treatment with or without the addition of carboplatin at a single institution. We assessed absolute neutrophil count recovery, incidence of neutropenia, neutropenic fever, antibiotic usage, treatment delays or discontinuation, dose reduction, and hospitalization with pegfilgrastim administration. Radiologists blinded to therapy reviewed CT scans to detect urinary tract inflammation.

Results—The median patient age was 69 years (range, 41–88 years), 78% were white, and 54% had a Gleason score ≥ 9 . Median overall survival was 9 months (95% confidence interval, 8–11). One patient (<1%) had neutropenia; 38 patients (25%) had infection. During cycle 1, a

Address for Correspondence: Jeri Kim, M.D., Department of Genitourinary Medical Oncology, Unit 1374, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, Texas 77030-3721, USA. Tel: +1-713-563-7237; Fax: +1-713-745-1625; jekim@mdanderson.org.

DISCLOSURE

The authors declare that they have no competing interests.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

significantly higher proportion of patients receiving pegfilgrastim after 24 hours developed infection than did those receiving pegfilgrastim the same day (26% vs. 6%, $P = 0.01$).

Conclusion—Same-day pegfilgrastim administration after cabazitaxel treatment with or without carboplatin in patients with mCRPC is feasible. The urinary tract inflammation rate (21%) was higher than that reported anecdotally. Results need to be prospectively validated.

Keywords

Prostate cancer; Pegfilgrastim; Safety; Cabazitaxel; Carboplatin; Urinary tract inflammation

Introduction

Cabazitaxel, a chemotherapy drug in the taxane family, is approved by the U.S. Food and Drug Administration for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC) after treatment with a front-line docetaxel-based regimen. Documented renal and urinary tract adverse effects of cabazitaxel include hematuria (17%), dysuria (7%), infections (8%), and urinary tract obstruction.¹ Bladder wall enhancement and ureteral enhancement have been observed anecdotally in patients being treated with this agent and are thought to be related to cystitis and ureteritis.² Interstitial cystitis has also been reported in patients receiving other taxanes³; however, the incidence and clinical significance of these findings have not been established.

Cabazitaxel is typically administered in the outpatient setting with a dose of pegfilgrastim given the subsequent day. Although guidelines from the National Comprehensive Cancer Network and the American Society of Clinical Oncology recommend that growth factor support be given 24 hours after the completion of therapy (day 2), they do recognize that in certain cases same-day pegfilgrastim may be considered.^{4, 5} In contrast to the standard day 2 schedule, a day 1 schedule is more convenient for patient care and reduces health care and patient expenditures. Same-day growth factor support has previously been reported in the literature.^{6–9}

We conducted a retrospective review of patients with mCRPC who were treated with cabazitaxel-based chemotherapy at The University of Texas MD Anderson Cancer Center. The objective of the study was to evaluate the safety of same-day dosing of pegfilgrastim after cabazitaxel, as determined by absolute neutrophil count recovery, and to assess the incidence of neutropenia, neutropenic fever, dose reduction, and treatment delays. We also investigated the frequency of cystitis and ureteritis, specifically as seen on routine staging CT scans during and/or after therapy.

Methods

Study Design

This study was approved by the Institutional Review Board at MD Anderson Cancer Center. Using Pharmacy Informatics at MD Anderson, we identified patients with mCRPC who received cabazitaxel treatment with or without carboplatin between September 2010 and September 2014. We excluded men who received this treatment while on clinical trial.

Patient Characteristics and Laboratory Data

Using the electronic health record, we undertook retrospective review of progress notes; pharmacy records; medication administration records; and baseline, serial, and follow-up radiographic reports. We collected patient demographics (date of birth, race/ethnicity), clinical and pathology data (height, weight, Eastern Cooperative Oncology Group performance status score, Gleason score), baseline laboratory results (prostate-specific antigen level [PSA], testosterone, liver function tests, alkaline phosphatase, lactate dehydrogenase [LDH], prostatic acid phosphatase, complete blood count [CBC], blood urea nitrogen [BUN], creatinine), medical history (location of metastases, previous chemotherapy treatments, prior prostatectomy, prior pelvic or prostatic brachytherapy or external beam radiotherapy), cabazitaxel regimen, pegfilgrastim regimen, absolute neutrophil count, positive cultures, antibiotic use, hospitalizations, reason for discontinuing cabazitaxel, and date of last follow-up and death.

Baseline and follow-up imaging studies, ordered per physician discretion, were reviewed for the presence of cystitis or ureteritis as evidenced by mucosal enhancement and wall thickening in the urinary tract. The reviewing radiologist was blinded to study intent. The date of radiological findings was correlated with the date of chemotherapy administration, symptoms of urinary tract infection or inflammation (dysuria, hematuria, lower abdominal pain, fever), subsequent treatment, and follow-up. We further correlated the findings with renal function, blood counts (for neutropenia/neutrophilia), blood and urine culture tests, and urine microscopy. Pathology results from any specimens collected from the urinary tract by endoscopic procedures were also recorded.

Statistical Considerations

Patient characteristics were summarized using descriptive statistics. Overall survival was defined as the time interval between treatment start date and death date, and patients who were alive were censored at the last follow-up date. The probabilities of overall survival were estimated using the Kaplan-Meier method. Fisher's exact test was used to investigate associations between infection and cabazitaxel treatment with or without the addition of carboplatin or pegfilgrastim administration as well as associations between urinary tract inflammation and these treatments. Statistical analyses were performed using SAS software, version 9.3 (SAS Institute, Cary, NC) and S-plus software (TIBCO Software, Palo Alto, CA).

Results

Characteristics of the 151 patients evaluated are shown in Table 1. Patient age ranged from 41 to 88 years, with a median of 69 years. The majority of patients were white (78%) and likely to have a Gleason score of 9 or above (9–10, 61%). Most patients had adenocarcinoma histology (96%), bone metastases (89%), and prior docetaxel therapy (83%). The median number of cycles of cabazitaxel treatment with or without carboplatin was 3 (range, 1–12). In Table 2 we summarize the clinical characteristic by cycle. Median overall survival was 9 months (95% confidence interval, 8–11 months) (Figure 1).

During cycle 1, a significantly higher proportion of patients receiving pegfilgrastim after 24 hours developed infection compared with those receiving pegfilgrastim the same day (26% vs. 6%, $P = 0.01$) (Table 3). Differences in subsequent cycles between timing of pegfilgrastim and the infection rate were not significant.

In cases with baseline and follow-up CT scans, 18/84 (21%) were positive for urinary tract inflammation. No correlation was observed between urinary tract inflammation detected on scans and timing of pegfilgrastim (Table 4). CT imaging of two patients who experienced urinary tract inflammation during the chemotherapy treatment demonstrates recovery after discontinuation of treatment (Figure 2).

Discussion

Our results demonstrate that day 1 pegfilgrastim administration after cabazitaxel treatment with or without carboplatin in patients with mCRPC is feasible. A significantly higher proportion of patients receiving pegfilgrastim after 24 hours (day 2) developed infection than did those receiving pegfilgrastim the same day (5/19 [26%] vs. 7/125 [6%]; $P = 0.01$). Furthermore, we observed that the rate of urinary tract inflammation rate in these patients (21%) was higher than that reported anecdotally, but no correlation was observed with the timing of pegfilgrastim administration.

Previously, neutropenia duration and febrile neutropenia incidence in patients receiving chemotherapy with pegfilgrastim administered the same day or 24 hours later have been compared in various clinical trials of breast cancer, lymphoma, and non-small cell lung cancer.⁶ Burris et al. showed that the absolute neutrophil count profile for same-day patients was earlier, deeper, and longer than that for next-day patients in the breast cancer and lymphoma studies.⁶ However, the results of same-day administration were not statistically inferior to those for next-day administration, according to neutropenia duration.⁶

In another randomized study, authors compared pegfilgrastim given on day 4 versus day 2 and found that administration of pegfilgrastim on day 4 was more effective in reducing severe leukocytopenias and resulted in fewer deaths during leukocytopenia.¹⁰ According to American Society of Clinical Oncology guidelines, there is evidence that pegfilgrastim administered 1 to 3 days after chemotherapy results in a lower risk of infection than pegfilgrastim administered on the same day as chemotherapy.¹¹ However, the guidelines also recommend that same-day pegfilgrastim not be prohibited if it provides the only feasible means of colony-stimulating factor administration for certain patients.¹¹

Cabazitaxel is a novel taxane approved for use after docetaxel administration in patients with mCRPC.¹² In a phase 3 open-label study, de Bono et al. showed that treatment with cabazitaxel plus prednisone improved overall survival in patients with mCRPC¹³ and reported that the most common clinically significant grade 3 or higher adverse events were neutropenia (82%), febrile neutropenia (8%), and diarrhea (6%).¹³ Currently, cabazitaxel is given with granulocyte colony-stimulating factor to prevent neutropenia. We reported the safety and lower rates of neutropenia in the patients who were treated with cabazitaxel with

or without carboplatin that received same-day pegfilgrastim. In addition to safety, it is also important for patient convenience.

In the literature, urinary tract inflammation has been reported anecdotally after cabazitaxel treatment, and the pathophysiology of this adverse effect is not clear.² In patients who were treated with cabazitaxel in the TROPIC study, 17% had hematuria of all grades.¹³ Grellety et al. reported on four patients who had cabazitaxel-induced hematuria and cystitis, and after finding all four patients had a history of pelvic radiation,² they suggested the patients' hematuria and cystitis could be attributed to a radiation recall syndrome. However, Kosaka and Oya reported a patient who developed hemorrhagic cystitis after cabazitaxel treatment for CRPC, and this patient had not received pelvic radiation therapy.¹⁴ In our cohort, the urinary tract inflammation rate (21%) was higher than that previously reported. We also reviewed records of the patients who developed urinary tract inflammation and found that only half (9/18) had a history of radiation therapy.

Limitations of this retrospective study include, first, that we did not document or rule out infection but rather relied on physician-transcribed documentation. Second, we did not perform serial CT scans to confirm that cystitis resolved after stopping chemotherapy. Currently, we are conducting a phase 2 clinical trial of cabazitaxel with or without carboplatin in patients with mCRPC (NCT01505868), with the intent to test our findings prospectively.

Acknowledgments

We thank Michael Worley from The University of Texas MD Anderson Cancer Center's Department of Scientific Publications for editing this manuscript. This work was supported in part by the National Institutes of Health through MD Anderson Cancer Center's Support Grant CA016672 (Clinical Trials Support Resource).

References

1. http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/201023s0151bl.pdf
2. Grellety T, Houede N, Hoepffner JL, Riviere J, Merino C, Lieutenant V, et al. Hemorrhagic cystitis in patients treated with cabazitaxel: a radiation recall syndrome? *Ann Oncol*. 2014; 25(6):1248–9. [PubMed: 24692580]
3. Wesolowski R, Peereboom D, Weiss P, Elson P, Thomas Budd G. Phase I trial of weekly docetaxel, weekly doxorubicin, daily oral cyclophosphamide, and G-CSF (ConTAC regimen) in advanced malignancies. *Invest New Drugs*. 2010; 28(4):502–8. [PubMed: 19434371]
4. National Comprehensive Cancer Network. Myeloid Growth Factors. V1.2016. NCCN Clinical Practice Guidelines in Oncology. [Accessed 5/2016]
5. Smith TJ, Khatcheressian J, Lyman GH, Ozer H, Armitage JO, Balducci L, et al. 2006 Update of recommendations for the use of white blood cell growth factors: an evidence-based clinical practice guideline. *J Clin Oncol*. 2006; 24(19):3187–205. [PubMed: 16682719]
6. Burris HA, Belani CP, Kaufman PA, Gordon AN, Schwartzberg LS, Paroly WS, et al. Pegfilgrastim on the same day versus next day of chemotherapy in patients with breast cancer, non-small-cell lung cancer, ovarian cancer, and non-Hodgkin's lymphoma: results of four multicenter, double-blind, randomized phase II studies. *J Oncol Pract*. 2010; 6(3):133–40. [PubMed: 20808556]
7. Skarlos DV, Timotheadou E, Galani E, Samantas E, Grimani I, Lianos E, et al. Pegfilgrastim administered on the same day with dose-dense adjuvant chemotherapy for breast cancer is associated with a higher incidence of febrile neutropenia as compared to conventional growth factor support: matched case-control study of the Hellenic Cooperative Oncology Group. *Oncology*. 2009; 77(2):107–12. [PubMed: 19622901]

8. Yardley DA, Burris HA 3rd, Farley CP, Barton JH, Peacock NW, Spiegel DR, et al. A phase II feasibility trial of dose-dense docetaxel followed by doxorubicin/cyclophosphamide as adjuvant or neoadjuvant treatment for women with node-positive or high-risk node-negative breast cancer. *Clin Breast Cancer*. 2008; 8(3):242–8. [PubMed: 18650154]
9. Gupta NKTS, Vanderhoff S, et al. Pegfilgrastim can be effectively administered the same day as chemotherapy to prevent neutropenia-related complications. *J Clin Oncol*, 2007 ASCO annual meeting proceedings part I. 2007; 25(185):1957.
10. Zwick C, Hartmann F, Zeynalova S, Poschel V, Nickenig C, Reiser M, et al. Randomized comparison of pegfilgrastim day 4 versus day 2 for the prevention of chemotherapy-induced leukocytopenia. *Ann Oncol*. 2011; 22(8):1872–7. [PubMed: 21292644]
11. Smith TJ, Bohlke K, Lyman GH, Carson KR, Crawford J, Cross SJ, et al. Recommendations for the use of WBC growth factors: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol*. 2015; 33(28):3199–212. [PubMed: 26169616]
12. National Cancer Institute. FDA approval for cabazitaxel. Bethesda, MD: National Cancer Institute; 2013. <http://www.cancer.gov/about-cancer/treatment/drugs/fda-cabazitaxel>
13. de Bono JS, Oudard S, Ozguroglu M, Hansen S, Machiels JP, Kocak I, et al. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. *Lancet*. 2010; 376(9747):1147–54. [PubMed: 20888992]
14. Kosaka T, Oya M. Hemorrhagic cystitis in a patient without a past history of radiation therapy who was treated with cabazitaxel for CRPC. *Ann Oncol*. 2015; 26(11):2355–6. [PubMed: 26347111]

Clinical Practice Points

- Cabazitaxel is FDA approved for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC) after treatment with a front-line docetaxel-based regimen and is typically administered in the outpatient setting with a dose of pegfilgrastim given the subsequent day.
- Although myeloid growth factors are commonly used to treat metastatic castration-resistant prostate cancer, the optimal timing of administration has not been well studied.
- We show that same-day pegfilgrastim administration after cabazitaxel treatment with or without carboplatin in patients with metastatic castration-resistant prostate cancer is feasible.
- The urinary tract inflammation rate after cabazitaxel treatment with or without carboplatin was higher than that reported anecdotally.
- Results need to be prospectively validated.

Figure 1.
Kaplan-Meier Estimates for Overall Survival. (Dotted lines represent boundaries of 95% confidence interval.)

Figure 2. Cranial Computed Tomographic Images of Two Patients Who Experienced Urinary Tract Inflammation. Patient 1, on February 9, 2012, with Ureteritis (A), and on April 20, 2013, with Resolved Ureteritis (B); Patient 2, on November 10, 2010, with Cystitis (C), and on May 11, 2012, with Resolved Cystitis (D).

Table 1

Summary of Patient Characteristics

Covariate	Characteristics	N (%) / Median (min, max)
Patients		151 (100)
Age (years)		69 (41, 88)
Height (cm)		176 (158, 192)
Weight (kg)		82 (44, 133)
BSA		2 (1.4, 2.6)
BMI		26 (16, 40)
Race	White	118 (78%)
	Black (African American)	20 (13%)
	Other	13 (9%)
Combined Gleason score	6	2 (2%)
	7	30 (23%)
	8	20 (15%)
	9	74 (56%)
	10	7 (4%)
	Missing	18 (12%)
Alkaline phosphatase		156 (41, 2452)
LDH		642 (44, 10202)
PAP	N=38	16.1 (0.5, 298)
ALT		21 (0, 165)
AST	N=139	30 (0, 215)
Total bilirubin	N=150	0.5 (0.2, 1.4)
PSA		89 (0.5, 2615)
Cycles per patient		3 (1, 12)
Pathology (adenocarcinoma)	Yes	145 (96%)
	No	6 (4%)
Pathology (ductal)	Yes	1 (1%)
	No	150 (99%)
Pathology (neuroendocrine)	No	151 (100%)
Pathology (other)	Yes	1 (1%)

Covariate	Characteristics	N (%) / Median (min, max)
	No	150 (99%)
Prior docetaxel chemotherapy	Yes	126 (83%)
	No	25 (17%)
Prior sipuleucel chemotherapy	Yes	7 (5%)
	No	144 (95%)
Prior investigational chemotherapy	Yes	2 (1%)
	No	149 (99%)
Other prior chemotherapy	0	51 (34%)
	1	37 (24%)
	2	30 (20%)
	3	16 (11%)
	>3	17 (11%)
Metastatic site of disease (bone)	Yes	134 (89%)
	No	17 (11%)
Metastatic site of disease (lymph node)	Yes	75 (50%)
	No	76 (50%)
Metastatic site of disease (visceral)	Yes	55 (36%)
	No	96 (64%)
Testosterone	< 20	133 (89%)
	≥20	9 (6%)
	Not recorded	8 (5%)
	Missing	1
ECOG PS	0	14 (9%)
	1	95 (63%)
	2	33 (22%)
	3	9 (6%)
Neutropenia during treatment	Yes	1 (1%)
	No	150 (99%)
Infection during treatment	Yes	38 (26%)
	No	113 (74%)
Urinary inflammation	Yes	18 (12%)
	No	133 (88%)

Abbreviations: min = minimum; max = maximum; BSA = body surface area; BMI = body mass index; LDH = lactate dehydrogenase; PAP = prostatic acid phosphatase; ALT = alanine aminotransferase; AST = aspartate aminotransferase; PSA = prostate-specific antigen; ECOG PS = Eastern Cooperative Oncology Group performance status.

Table 2

Clinical Characteristics by Cycle

Covariate		Cycle 1 (N = 151)	Cycle 2 (N = 116)	Cycle 3 (N = 85)	Cycle 4 (N = 61)
Neutropenia	Yes	0 (0%)	1 (1%)	0 (0%)	0 (0%)
	No	151 (100%)	111 (99%)	81 (100%)	59 (100%)
	Missing	0	4	4	2
Treatment	Cabazitaxel alone	122 (83%)	96 (87%)	68 (83%)	52 (88%)
	Cabazitaxel + carboplatin	25 (17%)	15 (13%)	14 (17%)	7 (12%)
	Missing	4	5	3	2
Pegfilgrastim	Within 24 hours	125 (83%)	85 (77%)	64 (78%)	48 (80%)
	Not within 24 hours	19 (13%)	17 (15%)	14 (17%)	10 (17%)
	Not given	6 (4%)	9 (8%)	4 (5%)	2 (3%)
	Missing	1	5	3	1
Infection	Yes	13 (9%)	13 (11%)	8 (9%)	6 (10%)
	No	138 (91%)	103 (89%)	77 (91%)	55 (90%)
Delay reason (low ANC)	No	151 (100%)	116 (100%)	85 (100%)	61 (100%)
Delay reason (infection)	Yes	2 (1%)	0 (0%)	1 (1%)	1 (2%)
	No	149 (99%)	116 (100%)	84 (99%)	60 (98%)
Delay reason (other)	Yes	3 (2%)	5 (4%)	3 (3%)	2 (3%)
	No	148 (98%)	111 (96%)	82 (97%)	59 (97%)
Delay reason (not treatment related)	Yes	0 (0%)	2 (2%)	0 (0%)	1 (2%)
	No	151 (100%)	114 (98%)	85 (100%)	60 (98%)
Dose reduction (low ANC)	Yes	0 (0%)	1 (1%)	1 (1%)	0 (0%)
	No	151 (100%)	115 (99%)	84 (99%)	61 (100%)
Dose reduction (infection)	Yes	0 (0%)	2 (2%)	1 (1%)	0 (0%)
	No	151 (100%)	114 (98%)	84 (99%)	61 (100%)

Covariate	Cycle 1 (N = 151)	Cycle 2 (N = 116)	Cycle 3 (N = 85)	Cycle 4 (N = 61)
Dose reduction (other)	Yes 0 (0%)	4 (3%)	1 (1%)	4 (7%)
	No 151 (100%)	112 (97%)	84 (99%)	57 (93%)
Hospitalization (low ANC)	Yes 1 (1%)	3 (3%)	0 (0%)	1 (2%)
	No 150 (99%)	113 (97%)	85 (100%)	60 (98%)
Hospitalization (infection)	Yes 9 (6%)	7 (6%)	2 (2%)	4 (7%)
	No 142 (94%)	109 (94%)	83 (98%)	57 (93%)
Hospitalization (other)	Yes 11 (7%)	4 (3%)	2 (2%)	1 (2%)
	No 140 (93%)	112 (97%)	83 (98%)	60 (98%)
Hospitalization (not treatment related)	Yes 5 (3%)	2 (2%)	3 (3%)	0 (0%)
	No 146 (97%)	114 (98%)	82 (97%)	61 (100%)
Treatment discontinuation (low ANC)	No 151 (100%)	116 (100%)	85 (100%)	61 (100%)
Treatment discontinuation (progressive disease)	Yes 20 (13%)	28 (24%)	17 (20%)	9 (15%)
	No 131 (88%)	88 (76%)	68 (80%)	52 (85%)
Treatment discontinuation (other)	Yes 7 (4%)	6 (5%)	5 (6%)	8 (13%)
	No 144 (96%)	110 (95%)	80 (94%)	53 (87%)

Abbreviation: ANC = Absolute neutrophil count.

Table 3

Comparison of Infection in Various Cycles

Cycle	Covariate	Specific Treatment/Time of Administration	Infection		P value
			Yes	No	
Cycle 1	Treatment	Cabazitaxel + carboplatin	4 (16%)	21 (84%)	0.12
		Cabazitaxel alone	8 (7%)	114 (93%)	
		Within 24 hours	7 (6%)	118 (94%)	
		Not within 24 hours	5 (26%)	14 (74%)	
Cycle 2	Treatment	Cabazitaxel + carboplatin	2 (13%)	13 (87%)	0.69
		Cabazitaxel alone	11 (11%)	85 (89%)	
	Pegfilgrastim	Within 24 hours	10 (12%)	75 (88%)	0.69
		Not within 24 hours	1 (6%)	16 (94%)	
Cycle 3	Treatment	Cabazitaxel + carboplatin	0 (0%)	14 (100%)	0.34
		Cabazitaxel alone	8 (12%)	60 (88%)	
		Within 24 hours	6 (9%)	58 (91%)	
		Not within 24 hours	1 (7%)	13 (93%)	
Cycle 4	Treatment	Cabazitaxel + carboplatin	0 (0%)	7 (100%)	1.00
		Cabazitaxel alone	6 (11%)	46 (89%)	
	Pegfilgrastim	Within 24 hours	6 (12%)	42 (88%)	0.58
		Not within 24 hours	0 (0%)	10 (100%)	

Note: P value was computed by Fisher's exact test.

Table 4

Comparison of Urinary Inflammation Various Cycles

Time	Covariate	Urinary inflammation		P value
		Yes	No	
Cycle 1	Treatment	Cabazitaxel + carboplatin	6 (24%)	0.04
		Cabazitaxel alone	11 (9%)	
	Pegfilgrastim	Within 24 hours	13 (10%)	
		Not within 24 hours	5 (26%)	
Cycle 2	Treatment	Cabazitaxel + carboplatin	6 (40%)	0.02
		Cabazitaxel alone	12 (12%)	
	Pegfilgrastim	Within 24 hours	12 (14%)	
		Not within 24 hours	3 (18%)	
Cycle 3	Treatment	Cabazitaxel + Carboplatin	4 (29%)	0.46
		Cabazitaxel alone	12 (18%)	
	Pegfilgrastim	Within 24 hours	13 (20%)	
		Not within 24 hours	3 (21%)	
Cycle 4	Treatment	Cabazitaxel + carboplatin	1 (14%)	1.00
		Cabazitaxel alone	10 (19%)	
	Pegfilgrastim	Within 24 hours	10 (21%)	
		Not within 24 hours	1 (10%)	

Note: P value was computed by Fisher's exact test.