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Real-world effectiveness of the pegfilgrastim on-body injector in preventing severe neutropenia

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Abstract

Introduction: Granulocyte colony-stimulating factors are used in medical oncology for the prevention of neutropenia. On-body injectors (OBI) have an advantage over the traditional injection (TI) method of not requiring a second visit to the clinic, but these devices are subject to failure. The objective of this study was to assess the efficacy of OBIs in the real-world.

Methods: Women with breast cancer diagnosed between June 2015 and June 2016 treated with cytotoxic chemotherapy and a granulocyte colony-stimulating factor were retrospectively identified from the medical records of Henry Ford Hospital. The primary outcome was the incidence of severe neutropenia (SN), defined as an absolute neutrophil count (ANC) $\leq$500. Secondary outcomes included incidence of neutropenia (ANC $\leq$ 1500), neutropenic fever, and mortality. A secondary analysis of the data was performed to identify predictors of SN.

Results: A total of 837 cycles of chemotherapy were analyzed. The OBI was used in 395 cycles and the TI in 442. The OBI group had patients that were older, had higher baseline ANC, and were more often white. The incidences of SN, neutropenic fever and neutropenia were not different between groups. Patients with a lower baseline ANC and white ethnicity were at a higher risk for SN. AC (doxorubicin and cyclophosphamide) was the most commonly used chemotherapy regimen (38% of total cycles).

Conclusions: There was no difference in the efficacy of the OBI and TI methods for preventing SN, neutropenic fever and neutropenia.

Keywords

Pegfilgrastim, G-CSF, neutropenia, on-body injector, real-world

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Introduction

Neutropenia is a common side effect of cytotoxic chemotherapy that can be seen with multiple different regimens used to treat cancer. The most feared complication of this adverse event is the development of neutropenic fever, which has serious implications in the setting of immunosuppression caused by chemotherapy.[1–3] Neutropenic fever has a significant impact on the prognosis of cancer patients, carrying a mortality that is reported to be up to 15% higher in those that develop it.[4,5]

Granulocyte colony-stimulating factors (GCSF) are widely used in medical oncology to prevent or treat neutropenia induced by chemotherapy.[1–3] The use of these agents is recommended when the estimated risk for neutropenia for a particular regimen of antineoplastic drugs exceeds 20%.[1,2] If the risk falls between 10% and 20%, it can be considered, and for a risk of less than 10%, they are not initially recommended.[1]

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Current recommendations are that GCSFs should be administered 24 hours after completion of the chemotherapy cycle, because same-day injections have been associated with the onset of neutropenia earlier and for a longer duration after the infusion.[1,2,6] An on-body injector (OBI) of pegfilgrastim (Neulasta Onpro) has been released to the market in 2014 by Amgen (Thousand Oaks, CA) and has been used interchangeably with the traditional method depending on patient preference and insurance coverage.[7] The device is implanted subcutaneously on the day of chemotherapy and is timed to deliver the GCSF approximately 27 hours after.[7]

Since the introduction of the OBI method, a few concerns have been raised. One of these concerns is mechanical problems with the device resulting in a failure to deliver the medication. Failure rates of 1.7%–6.9% have been previously reported.[7–10] However, it is unclear if these failures translate into a clinically significant adverse event. A study by Townley et al reported a failure rate of 6.9% but no significant difference in the incidence of neutropenia.[10] The objective of our study was to identify if patients receiving OBI would have a higher risk of developing severe neutropenia (SN) when compared with those that received traditional injections (TI) in the day following chemotherapy in a real-world clinical setting.

Material and methods

Patients

Adult women diagnosed with breast cancer between June 2015 and June 2016 and treated with cytotoxic chemotherapy were identified retrospectively from the medical records of Henry Ford Hospital (Detroit, MI). We restricted our sample to breast cancer patients to maintain its homogeneity and because these patients often receive cytotoxic chemotherapy that require GCSF agents. All cycles of chemotherapy in which the patient received a GCSF were included in the study. Information collected included patient demographics, treatment regimens, breast cancer specific information (histology, hormone receptor status, and HER-2 status), GCSF administration method, absolute neutrophil counts (ANC), incidence of neutropenic fever and mortality. Cycles were divided into two study groups depending on the method of administration of GCSF: TI or OBI. The study was approved by the Henry Ford Health System Institutional Review Board (#00000253) and conducted according to the principles of the Declaration of Helsinki. A waiver of consent was granted by the institutional review board due to the retrospective nature of the study.

Outcome measures

Neutropenia, SN, neutropenic fever and infection-related mortality were outcomes measured to assess the efficacy of each method of GCSF administration. Each outcome was assessed after each cycle of chemotherapy in which the patients received GCSFs. Neutropenia and SN were defined as an ANC of 1500 or less and 500 or less, respectively, after a cycle of chemotherapy. Post-chemotherapy ANC was assessed by taking the lowest value (nadir) between two cycles or up to 30 days after the last cycle. Neutropenic fever was identified by looking for clear documentation of such in the patient's chart. Each episode of neutropenic fever was associated with the chemotherapy cycle responsible for the patient's neutropenia and the GCSF administration method for that cycle. Infection-related mortality was defined as death attributed to infection (or febrile neutropenia) as a direct or underlying cause (infection being what initiated the sequence of events leading to death).

Statistical analysis

Continuous variables were expressed as mean ± standard deviation. Categorical variables were expressed as frequency and percentage. As each chemotherapy cycle was nested within patients, multilevel models with clustering on patients were performed for multilevel analyses. Youden index was used to examine the optimal cutoff of baseline ANC. Univariate analysis was used to screen for predictors potentially associated with high risk for SN. Predictors with $p < 0.15$ in the univariate analyses were selected for multivariate multilevel logistic regression analysis. Odds ratio was calculated with the corresponding 95% CI. A two-sided $p < 0.05$ was considered statistically significant. All statistical analyses were performed with SAS 9.4 (SAS Institute, Cary, NC).

Results

Our study comprised a total of 182 patients and 837 cycles of chemotherapy with GCSF injections. A comparison of the baseline characteristics and chemotherapy regimens used are summarized in Table 1. The OBI was used in 395 cycles while the TI method was used in 442 cycles. All patients in the study were female. The OBI group cycles comprised a majority of white patients (69.4%), while the TI group had a majority of black patients (52.7%). The majority of patients in the sample had hormone-receptor positive (ER positive in 67.6% and PR positive in 52.7%) and HER-2 negative tumors (only 30.9% had a HER-2 mutation). The OBI group had more cycles of chemotherapy with patients

Table 1. Baseline characteristics of patients in the chemotherapy cycles of each group.

Characteristic	All cycles (n = 837)	On body (n = 395)	Traditional (n = 442)	P Value
Female sex, N (%)	837 (100.0%)	395 (100.0%)	442 (100.0%)	
Age, years (mean ± SD)	57.5 ± 11.7	58.5 ± 11.3	56.6 ± 12.0	<0.001
Race, N (%)				<.0001
White	466 (55.7%)	274 (69.4%)	192 (43.4%)	
Black	354 (42.3%)	121 (30.6%)	233 (52.7%)	
Other	17 (2.0%)	0	17 (3.9%)	
Body surface area, m^2 (mean ± SD)	1.8 ± 0.2	1.8 ± 0.2	1.9 ± 0.2	<0.001
CCI (mean ± SD)	1.0 ± 1.8	1.0 ± 1.8	0.9 ± 1.7	<0.001
ECOG				0.30
0	561 (67.4%)	240 (60.8%)	321 (73.5%)	
1	238 (28.6%)	133 (33.7%)	105 (24.0%)	
2	23 (2.8%)	16 (4.1%)	7 (1.6%)	
3	10 (1.2%)	6 (1.5%)	4 (0.9%)	
Smoking	397 (47.4%)	214 (54.2%)	183 (41.4%)	0.072
Estrogen receptor positive	557 (66.6%)	287 (72.7%)	270 (61.2%)	0.047
Progesterone receptor positive	424 (50.7%)	224 (56.7%)	200 (45.4%)	0.065
HER-2 positive	288 (35.6%)	124 (31.4%)	164 (37.5%)	0.38
ANC (mean ± SD)	6186.9 ± 3732.8	6683.5 ± 4217.8	5743.2 ± 3178.4	0.025
Number of chemotherapy cycles (mean ± SD)	5.8 ± 3.8	6.4 ± 4.8	5.3 ± 2.6	0.56
Length of chemotherapy cycle (mean ± SD)	20.2 ± 6.2	20.3 ± 6.2	20.1 ± 6.2	0.73
Chemotherapy regimen				
AC (doxorubicin and cyclophosphamide)	318 (38.0%)	142 (35.9%)	176 (39.8%)	
TC (docetaxel and cyclophosphamide)	202 (24.1%)	99 (25.0%)	103 (23.3%)	
TCHP (docetaxel, carboplatin, trastuzumab and pertuzumab)	101 (12.0%)	39 (9.9%)	62 (14.0%)	
TCH (docetaxel, carboplatin and trastuzumab)	110 (13.1%)	59 (14.9%)	51 (11.5%)	
THP (docetaxel, trastuzumab and pertuzumab)	34 (4.0%)	21 (5.3%)	13 (2.9%)	
TAC (docetaxel, doxorubicin and cyclophosphamide)	24 (2.8%)	13 (3.3%)	11 (2.5%)	
Paclitaxel	18 (2.1%)	10 (2.5%)	8 (1.8%)	
Other regimens	30 (3.6%)	12 (3.0%)	18 (4.0%)	

ANC, absolute neutrophil count; CCI, Charlson Comorbidity index; ECOG, Eastern Cooperative Oncology Group; SD, standard deviation.

with ER positive tumors, but there was no difference in PR positive and HER-2 positive tumors. The OBI group had more patients with Eastern Cooperative Oncology Group (ECOG) performance scores of 2 or 3 when compared to the TI group, but that difference was not statistically significant ($p = 0.3$). No patients had an ECOG of 4. The comorbidity profile, as illustrated by the Charlson Comorbidity Index, and the smoking rate were similar between the groups.

The mean ANC before each cycle of chemotherapy was higher in the OBI group, 6638.5 vs. 5743.2 in the TI group ($p = 0.025$). There was no difference in the rates of neutropenia (26.5% in the OBI group vs. 29.5% in the TI group, $p = 0.51$) and SN (11.7% OBI vs. 12.0% TI, $p = 0.92$) between the study groups. The overall rate of SN in the sample was 11.9%. Only 6 patients developed neutropenic fever, 5 in the TI group and 1 in the OBI group. The difference was not statistically significant ($p = 0.13$). No patients in our study had infection-related mortality.

The OBI method had mechanical failures in 5 cycles (1.26%) of 5 different patients. In 2 occasions, the device fell off before a dose was administered. One of the patients whose device fell off received a TI and despite that developed SN in that cycle. The other patient had a new OBI placed and did not develop neutropenia. One patient experienced a leak of the medication during the injection and received a subsequent TI with no complications. Two patients reported that the device failed to administer the medication. One of these patients developed SN and received filgrastim daily for 5 days. Her next chemotherapy cycle was delayed. The other patient that inappropriately did not receive the OBI dose developed neutropenia (not severe) and also had the following cycle delayed, but received no other GCSF.

Table 2 demonstrates the characteristics of patients that developed SN compared to those who did not. Patients were more likely to develop SN if they were white. The strongest predictor of SN was the baseline ANC (mean of 4878.9 in those who developed it vs.

Table 2. Predictors of severe neutropenia.

Variable	ANC > 500 (n = 735)	ANC ≤ 500 (n = 99)	OR (95% CI)	P Value
Age, years (mean ± SD)	57.5 ± 11.9	57.6 ± 9.9	0.995 (0.94–1.05)	0.84
Race, N (%)				0.022
White	393 (53.5%)	72 (72.7%)	ref	
Black	330 (44.9%)	22 (22.2%)	0.22 (0.07–0.73)	
Other	12 (1.6%)	5 (5.0%)	4.32 (0.19–101)	
BSA, m^2 (mean ± SD)	1.9 ± 0.2	1.8 ± 0.2	0.11 (0.01–1.98)	0.135
CCI (mean ± SD)	1.0 ± 1.8	0.6 ± 1.0	0.72 (0.48–1.08)	0.109
ECOG, N (%)				0.85
0 or 1	701 (95.3%)	95 (95.9%)	ref	
2 or higher	29 (3.9%)	4 (5.0%)	1.33 (0.06–27.97)	
Smoking	351 (47.8%)	45 (45.5%)	0.91 (0.28–2.94)	0.87
Estrogen receptor positive	493 (67.2%)	61 (61.6%)	0.72 (0.21–2.49)	0.60
Progesterone receptor positive	379 (51.6%)	44 (44.4%)	0.67 (0.21–2.16)	0.50
HER-2 positive	260 (35.6%)	28 (28.3%)	28 (28.3%)	0.15
Baseline ANC (mean ± SD)	6372.0 ± 3835.1	4878.9 ± 2542.8	0.98 (0.96–0.99)	<0.001
Number of chemotherapy cycles (mean ± SD)	5.9 ± 4.0	5.1 ± 2.3	0.89 (0.74–1.07)	0.21
Length of chemotherapy cycle, days (mean ± SD)	20.3 ± 6.3	19.5 ± 5.3	1.02 (0.96–1.08)	0.52

ANC, absolute neutrophil count; BSA, body surface area; CCI, Charlson Comorbidity index; ECOG, Eastern Cooperative Oncology Group; OR, odds ratio; ref, reference; SD, standard deviation.

6372 in those who did not, $p < 0.001$). However, prior ANC had a poor capability of predicting SN (Figure 1). Using a cutoff of 4605, baseline ANC had a sensitivity of 62.6% and a specificity of 60.1% for predicting the development of SN. Age, body surface area, Charlson Comorbidity Index, number of chemotherapy cycles, ECOG scores and smoking were not associated with the development of SN.

AC (doxorubicin and cyclophosphamide) was the most commonly used regimen in either group, followed by TC (docetaxel and cyclophosphamide). TAC (docetaxel, doxorubicin and cyclophosphamide) was the regimen with the highest rates of SN (41.7%), but it was only used in 2.86% of the chemotherapy cycles. SN was noted in 16.4% of the cycles using AC. A multivariate analysis (Table 3) showed that white ethnicity (compared to black) and lower baseline ANC were independent predictors of SN. The difference in SN rates compared between TAC and AC was not statistically significant ($p = 0.084$). TCH (docetaxel, carboplatin and trastuzumab) and TCHP (docetaxel, carboplatin, trastuzumab and pertuzumab) regimens had a similar incidence of SN compared to AC in the multivariate analysis, while TC had a lower incidence. No patients that received THP (docetaxel, trastuzumab and pertuzumab) developed SN.

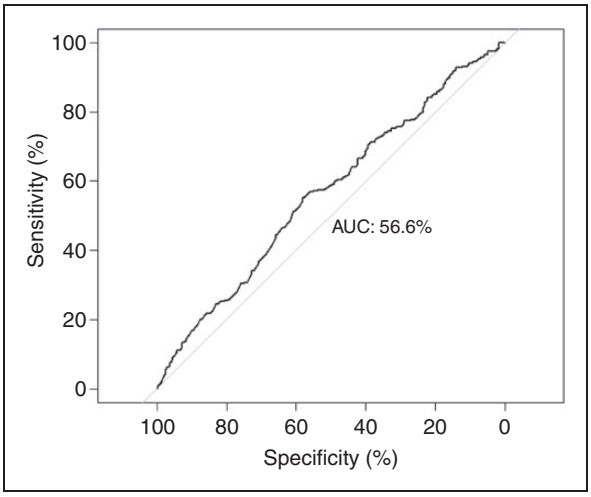

Figure 1. Sensitivity and specificity of baseline ANC < 4605 to predict severe neutropenia. Abbreviations: ANC, absolute neutrophil count; AUC, area under the curve.

Discussion

This study demonstrates no significant difference in clinical outcomes for patients that received GCSF via TI and OBI in a real-world clinical setting. The main purpose of using GCSFs in cancer care is to prevent neutropenia and its deadly complication, neutropenic fever, both of which had a similar incidence in our study groups. However, there were differences noted between the two study groups, which is one of the major limitations of a retrospective study. It is possible that both clinicians and patients would favor the OBI method in the setting of transportation or mobility difficulties to avoid the burden of a next-day visit, given

Table 3. Multivariate analysis of predictors of severe neutropenia.

Variables	Odds ratio	95% Confidence Limits		P value
Other regimens vs AC	0.020	0.001	0.368	0.009
TAC vs AC	12.055	0.716	203	0.084
TC vs AC	0.257	0.070	0.944	0.041
TCH vs AC	1.004	0.216	4.659	0.996
TCHP vs AC	0.227	0.045	1.158	0.074
Black vs White	0.308	0.101	0.938	0.038
Other race vs White	3.425	0.182	64	0.410
BSA	0.203	0.015	2.730	0.229
CCI	0.774	0.516	1.161	0.216
Baseline ANC	0.974	0.960	0.988	<0.001

AC, doxorubicin and cyclophosphamide; ANC, absolute neutrophil count; BSA, body surface area; CCI, Charlson Comorbidity index; TAC, docetaxel, doxorubicin and cyclophosphamide; TC, docetaxel and cyclophosphamide; TCH, docetaxel, carboplatin and trastuzumab; TCHP, docetaxel, carboplatin, trastuzumab and pertuzumab.

that this group was comprised of older patients. This is supported by a study performed by Hauber et al, in which the authors reported that 49.5% of physicians opted for the OBI among clinically compromised patients, while for less compromised patients, the OBI was chosen in only 28% of occasions.[11] It should also be noted that patients in the TI group had a lower baseline ANC and a higher proportion of white patients, which could translate into a higher risk of developing SN with chemotherapy, as discussed later in this section.

Overall our results are similar to data available in the literature. A study published by Townley et al compared the incidence of grade 4 neutropenia in patients that received GCSF either via an OBI or manual injection. The sample comprised 116 patients and no difference was found (5.2% of patients developed the outcome in the OBI group and 1.7% in the manual injection group, $p = 0.61$).[10] Other data available on this subject comes from abstracts. A study by Ng et al with a larger sample ($n = 326$) reported no difference in the rates of febrile neutropenia (7.7% in the OBI group and 7.2% in the TI group, $p = 0.86$),[12] Jindal et al also looked into febrile neutropenia rates in a group of 120 patients, reporting that 14% in the manual injection group and 8.3% in the OBI group developed the outcome ($p = 0.17$).[13]

There are significant differences between the aforementioned studies and our study. Our data is reported counting each chemotherapy cycle as a subject, while other studies count each patient as a subject. In our view, analyzing each chemotherapy cycle is more indicative of each method's individual failures since those are applied prior to each cycle to prevent the neutropenia that is expected 10–14 days after chemotherapy.[1,2,14] It also eliminates the possibility of patients that used both methods during their chemotherapy course being analyzed as belonging to a single group. Furthermore, it prevents situations in which a patient has received GCSF during most, but not all, chemotherapy cycles. This might account for the significantly lower rates of febrile neutropenia observed in our study when compared to Ng et al and Jindal et al.[12,13] However, the study by Townley et al described only 1 patient in their sample that developed febrile neutropenia, which is more consistent with our findings.[10] Another explanation for this difference is that our study only included breast cancer patients, which accounted for the majority of patients in Townley et al (63.8%), but only 31.6% of patients in Jindal et al and 41.6% in Ng et al.[10,12,13] The latter two studies also had a significantly higher proportion of patients with non-Hodgkin's lymphoma, which has been previously described to carry a higher risk of grade 3 or 4 neutropenia than breast cancer.[12,13,15]

Regarding mechanical failures of the OBI, our study revealed a failure rate of only 1.26%, which is lower than the previously reported rates of 1.7%–6.9%.[7–10] One of the reasons for this is that each chemotherapy cycle was counted as a subject, as already mentioned. Out of the 5 cycles that had a device failure reported, neutropenia developed in 3, and 2 of these had SN. No subjects died or developed neutropenic fever after an OBI failure. In spite of the device failures and the possible higher risk of participants of the OBI group (due to white race and lower ANC), the overall incidence of neutropenia and SN was not different between groups. This indicates that the device failure rate is not high enough to have a significant clinical impact. However, it should be noted that in 4 out of the 5 failures patients received either a new device or a GCSF injection with manually prefilled syringes (TI).

On a secondary analysis, we demonstrated that white race and lower baseline ANC were independently

associated to the development of SN, even when adjusting for the different chemotherapy regimens used. Low baseline ANC was previously described as a risk factor in the literature. Lyman et al performed a systematic review and described that age, performance status, nutritional status, chemotherapy dose intensity and baseline ANC were associated to SN and febrile neutropenia.[16] The same author published an updated systematic review and described similar risk factors associated with febrile neutropenia, but also reported advanced disease, certain comorbidities (mainly cardiovascular and renal diseases) and specific genetic polymorphisms.[17] Other risk factors mentioned in the literature include both absence and presence of concomitant radiotherapy, low body surface area, chemotherapy regimen, number of chemotherapy cycles, high p75-RTNF levels, low serum albumin, high serum LDH and low platelet counts.[15–20] Some studies have previously correlated white race with a higher risk for SN and febrile neutropenia during chemotherapy, although it has also been reported that black patients experience more treatment delays due to lower leukocyte counts both prior and after chemotherapy.[21–23] Therefore, it is unclear if race influences the risk of neutropenic complications during chemotherapy.

In conclusion, pegfilgrastim delivered via OBI seems to be equally effective to the TI method in preventing neutropenia, SN and febrile neutropenia in a real-world clinical setting. Although device failures were observed in the OBI group and most patients developed neutropenia after a failure, the low frequency of these events did not result in a significant difference in the study outcomes. Patients with a lower baseline ANC seem to be at higher risk of developing SN despite the use of GCSFs. White ethnicity may also be a risk factor for SN despite higher ANC counts in this ethnic group when compared to black, but current data is conflicting.[24] Future studies are needed to address the cost-effectiveness of the OBI method, but otherwise clinicians should feel safe using it as an alternative to the TI method for patients that appreciate the convenience of not having to return to clinic for a next-day visit.

Declaration of Conflicting Interests

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References

1. Becker PS, Griffiths EA, Alwan LM, et al. NCCN guidelines insights: hematopoietic growth factors, version 1.2020. *J Natl Compr Canc Netw* 2020; 18: 12–22.
2. Smith TJ, Bohlke K, Lyman GH, et al. Recommendations for the use of WBC growth factors: American society of clinical oncology clinical practice guideline update. *J Clin Oncol* 2015; 33: 3199–3212.
3. Bennett CL, Djulbegovic B, Norris LB, et al. Colony-stimulating factors for febrile neutropenia during cancer therapy. *N Engl J Med* 2013; 368: 1131–1139.
4. Lalami Y and Klastersky J. Impact of chemotherapy-induced neutropenia (CIN) and febrile neutropenia (FN) on cancer treatment outcomes: an overview about well-established and recently emerging clinical data. *Crit Rev Oncol Hematol* 2017; 120: 163–179.
5. Lyman GH, Michels SL, Reynolds MW, et al. Risk of mortality in patients with cancer who experience febrile neutropenia. *Cancer* 2010; 116: 5555–5563.
6. Burris HA, Belani CP, Kaufman PA, 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: 133–140.
7. Mahler LJ, DiBlasi R, Perez A, et al. On-body injector: an administration device for pegfilgrastim. *Clin J Oncol Nurs* 2017; 21: 121–122.
8. Joshi RS, Egbuna OI, Cairns AS, et al. Performance of the pegfilgrastim on-body injector as studied with placebo buffer in healthy volunteers. *Curr Med Res Opin* 2017; 33: 379–384.
9. Stuessy P, Sanchez FA and Schober M. Retrospective review of pegfilgrastim on-body injector delivery rates in a large health system [abstract]. *J Clin Oncol* 2017; 35: e18273.
10. Townley C, Porter C and McMullen N. Comparing grade 4 neutropenia associated with pegfilgrastim administered via the onpro device versus manual injection with a prefilled syringe. *J Hematol Oncol Pharm* 2018; 8: 119–125.
11. Hauber AB, Mange B, Price MA, et al. Administration options for pegfilgrastim prophylaxis: patient and physician preferences from a cross-sectional survey. *Support Care Cancer* 2018; 26: 251–260.
12. Ng H, Douce D, Byington A, et al. Man vs machine: are febrile neutropenia rates different using an in-clinic vs on-body injection [abstract]? *J Clin Oncol* 2018; 36: e18867.
13. Jindal A, Kover J, Raduka V, et al. Incidence of neutropenic fever at a safety net hospital in cancer chemotherapy patients receiving prophylactic pegfilgrastim manual injection compared to the on-body auto-injector [abstract]. *Blood* 2018; 132: 4709.
14. Moore DC. Drug-induced neutropenia: a focus on rituximab-induced late-onset neutropenia. *P T* 2016; 41: 765–768.
15. Lee M, Yee J, Kim JY, et al. Risk factors for neutropenia and febrile neutropenia following prophylactic pegfilgrastim. *Asia Pac J Clin Oncol* 2019; 15: 231–237.

16. Lyman GH, Lyman CH and Agboola O. Risk models for predicting chemotherapy-induced neutropenia. *Oncologist* 2005; 10: 427–437.
17. Lyman GH, Abella E and Pettengell R. Risk factors for febrile neutropenia among patients with cancer receiving chemotherapy: a systematic review. *Crit Rev Oncol Hematol* 2014; 90: 190–199.
18. Schwenkglenks M, Jackisch C, Constenla M, et al. Neutropenic event risk and impaired chemotherapy delivery in six European audits of breast cancer treatment. *Support Care Cancer* 2006; 14: 901–909.
19. Intragumtornchai T, Sutheesophon J, Sutcharitchan P, et al. A predictive model for life-threatening neutropenia and febrile neutropenia after the first course of CHOP chemotherapy in patients with aggressive non-Hodgkin's lymphoma. *Leuk Lymphoma* 2000; 37: 351–360.
20. Voog E, Bienvenu J, Warzocha K, et al. Factors that predict chemotherapy-induced myelosuppression in lymphoma patients: role of the tumor necrosis factor ligand-receptor system. *J Clin Oncol* 2000; 18: 325–331.
21. Plaxe SC, Brooks SE, Tian C, et al. Influence of race on tolerance of platinum-based chemotherapy and clinical outcomes in women with advanced and recurrent cervical cancer: a pooled analysis of 3 gynecologic oncology group studies. *Am J Obstet Gynecol* 2008; 199: 539.e1-6.
22. Laskey R, Poniewierski M, Lopez M, et al. Predictors of severe and febrile neutropenia during primary chemotherapy for ovarian cancer [abstract]. *Gynecol Oncol* 2011; 120: S74–S75.
23. Hershman D, Weinberg M, Rosner Z, et al. Ethnic neutropenia and treatment delay in African American women undergoing chemotherapy for early-stage breast cancer. *J Natl Cancer Inst* 2003; 95: 1545–1548.
24. Bain BJ. Ethnic and sex differences in the total and differential white cell count and platelet count. *J Clin Pathol* 1996; 49: 664–666.