

## Assessing the Value of Weekly Full Blood Counts in Patients with Gynecological Cancers Receiving Weekly Carboplatin/Paclitaxel Chemotherapy

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### Abstract

**Background:** Dose dense carboplatin and paclitaxel regimens are increasingly being used to treat advanced serous gynaecological malignancies (ovary and uterus) in the adjuvant and relapse setting. The purpose of this study was to quantify the incidence of neutropenia and thrombocytopenia in patients receiving weekly Carboplatin and Paclitaxel (wCP) or Carboplatin q21 with weekly Paclitaxel (CwP) and more specifically the incidence of clinically significant myelosuppression – neutropenic sepsis or thrombocytopenia requiring intervention such as platelet transfusion. Our overall aim being to determine if routine blood counts are really necessary on days 8 and 15 of a wCP 21/28 day cycle or CwP 21 day cycle.

**Results:** We analysed haematological data for 56 patients, 24 of whom had wCP and received 179 planned infusions and 32 of whom had CwP and received 407 planned infusions. The incidence of >G3 neutropenia in the group receiving wCP was 2.8% (5/179), the incidence of >G3 thrombocytopenia was 1.8% (3/179). Patients receiving CwP had an incidence of >G3 neutropenia and >G3 thrombocytopenia of 0.7% (3/407). Notably, there was only one case of febrile neutropenia, incidence of 0.2% (1/407).

**Conclusion:** Gynaecological patients receiving either wCP or CwP regimens do not require routine full blood counts on day 8 and 15. This allows a more cost effective and efficient route of chemotherapy delivery for both patients and staff.

**Keywords:** Dose dense chemotherapy; Serous ovarian cancer; Papillary serous uterine cancer; Weekly paclitaxel; Febrile neutropenia; Thrombocytopenia; Full blood count

### Introduction

Ovarian cancer is the leading cause of mortality of all gynecological cancers [1]. The majority of patients with ovarian cancer present at an advanced stage with most of these relapsing despite debulking surgery and first line platinum chemotherapy. The choice of the most appropriate second line therapy to offer patients is determined by the Platinum Free Interval (PFI), defined as the time from the last chemotherapy to the decision to treat again. The PFI has been shown to be a reasonable indicator of the likelihood of a patient's response to further platinum based chemotherapy. The longer the PFI the greater the chance of subsequent response [2,3]. Using this paradigm, Relapsed Ovarian Cancer (ROC) patients can be divided into platinum sensitive or platinum resistant populations where those who have a PFI of 6months or more are deemed platinum sensitive and those whom have a PFI less than 6 months are platinum resistant.

Unfortunately, in patients with platinum resistant/refractory tumours, response rates even to non-platinum agents are poor, ranging from 6-29% with agents such as gemcitabine and liposomal doxorubicin [3,4]. Thus with this group of patients in mind, dose dense chemotherapy regimens have been developed to treat ROC with the aim of increasing treatment intensity by raising the duration of exposure to chemotherapy rather than escalating the dose. The most common dose dense regimens reported in the literature include

weekly cisplatin with etoposide and weekly carboplatin/paclitaxel [5-8]. Weekly therapy is generally given for three consecutive weeks with an optional week off (i.e either q21d or q28d), where patients can either receive weekly carboplatin and paclitaxel wCP or 3-4 weekly carboplatin with weekly paclitaxel, for 3 of any 4 week cycle CwP. Given this way, dose dense platinum doublets can achieve favourable response rates in both platinum sensitive (93.3-100%) and platinum resistant/refractory (37.5-60%) patients. Dose dense therapy has also been used in first-line ovarian cancer where in Japanese patients it has been shown to improve both progression free and overall survival [9]. The ICON 8 trial is aiming to corroborate this finding.

In the early studies of carboplatin, the dose limiting toxicity was noted to be myelosuppression affecting platelets more than leukocytes. The clearance of carboplatin is linearly proportional to glomerular filtration rate and the half-life between 2 and 6 hours in patients with normal renal function. Dosing has therefore evolved to relate to an area under the concentration-time curve (AUC) and both toxicity and response suggest that this relationship is safe and pragmatic. Not only is there a relationship between myelosuppression and AUC, the higher the AUC the greater the myelotoxicity [10], but patients already treated with platinum analogues have been shown to develop a greater degree of myelosuppression from any given AUC [11]. Given the AUC-effect relationships described above a number of studies have been performed to develop models to describe the relationship between both dose and AUC and dose and platelet nadir. In adults, perhaps the most common method is that of Calvert which describes the relationship between dose and AUC [12]. There is no evidence that increasing the AUC to above a level of 5 (using EDTA GFR estimates)

or 6 (using Cockcroft-Gault calculated GFR) in ovary cancer patients results in any better responses or overall survival [13]. Having established reasonable safety with routine doses of platinum therapy, we do not 'routinely' assess nadir blood counts in these patients.

Amongst the published data relating to combination carboplatin and paclitaxel, the platelet-sparing effect is well recognized [14]. It is thought that it antagonises the effect of carboplatin on the megakaryocytes and thus "spares" the thrombocytopenia associated with carboplatin usage [15]. This platelet-sparing effect of paclitaxel has also been reported in heavily pretreated patients [16,17]. Routine practice in the delivery of cytotoxics has involved checking the blood count prior to the delivery of any cytotoxic drug, but from the early phase studies of carboplatin and the published experience with weekly paclitaxel alone, we postulated that the blood count only requires checking every 3-4 weeks, provided such patients are not obviously unwell. Thus we sought to quantify the incidence of thrombocytopenia and neutropenia in this population, in particular to determine if routine full blood counts (FBC) were really necessary on days 8 and 15, of each 21/28 day cycle, provided patients were clinically fit enough for chemotherapy.

## Materials and Methods

From our gynecological cancer chemotherapy database, we retrospectively identified 56 patients who received treatment between December 2008 and 2011 with either weekly carboplatin and weekly paclitaxel (wCP) or three weekly carboplatin and weekly paclitaxel (CwP). These broadly fell into two groups: 24 received wCP and were treated between December 2008 and January 2010, for advanced ovarian and papillary serous uterine carcinoma and 32 received CwP and were treated between February 2010 and December 2011. No patient received GCSF as we do not routinely use this, reserving it only for patients who have repeated neutropenic septic episodes.

Of the first group (weekly carboplatin and weekly paclitaxel wCP), 3 were chemo-naïve, and treatment was planned on days 1, 8 and 15 within a 28 day cycle – i.e. they did not receive wCP on day 21. Blood counts had been done weekly, prior to each planned infusion of chemotherapy, on all these patients and this haematological data was identified and recorded. Patients were medically reviewed each week and were required to have a platelet count of  $>100 \times 10^9$  L and neutrophils of  $>1 \times 10^9$  L as well as being clinically 'fit enough' to proceed with each week's treatment.

By contrast, of the 32 patients receiving (three weekly carboplatin and weekly paclitaxel CwP), 27 were chemo naïve, and paclitaxel was

administered on days 1, 8 and 15 of a 21 day cycle with carboplatin given on day 1 alone. In the light of the toxicity data from Katsumata et al where there was an equal incidence of febrile neutropenia in both three weekly and weekly arms of first-line chemotherapy [9] medical review and blood counts for these 32 patients were only performed on the first day of each 21 day cycle, akin to routine patients receiving standard three weekly carboplatin/paclitaxel combinations. Chemotherapy nurses administering the weekly paclitaxel alone on days 8 or 15 were free to refer any patient deemed 'unwell' for medical review and or blood tests. Haematological data were identified and recorded for each patient as well as any other blood counts done within any of the treatment cycles administered to assess the frequency of extra blood sampling and the impact of omitting d8 and d15 blood checks. Review of all 56 patient notes was undertaken to document any other treatment related haematological toxicity.

## Results

Of the 24 patients who received wCP, 21 had advanced serous ovarian cancer and 3 had serous uterine carcinoma, 193 infusions were planned. These 21 patients had previously received between 1 and 6 previous lines of chemotherapy (mean 2.5). The mean number of consecutive weeks of treatment given was 8 (range 1-12, median 7.5). A total of 14 infusions were omitted for reasons unrelated to haematological parameters and therefore these were excluded from the study sample leaving 179 infusions. Table 1 demonstrates the study population and chemotherapy regimens they received whilst Table 2 depicts the number of lines of previous chemotherapy treatments the patients had received in the wCP group. Of the chemotherapy naïve patients who received wCP, 2 patients had dose dense chemotherapy as first line treatment with associated interval debulking and one patient had first line adjuvant therapy for uterine carcinoma. The incidence of neutropenia was 2.8% (5/179), occurring on 5 occasions in 3 patients. One patient who received wCP with a carboplatin dose based on AUC 3, had grade 3 neutropenia at day 8 of every cycle. Two patients who received wCP with a carboplatin dose based on AUC 2.5 had grade 3 neutropenia ( $0.9$  and  $0.7 \times 10^9$  L) at day 15 of one cycle. There were no instances of febrile neutropenia in this group. The incidence of thrombocytopenia was 1.8%. There were 3 occasions where thrombocytopenia occurred (3/179). These were detected on day 1 in 2 patients, all cases were grade 2 thrombocytopenia. One patient proceeded to have day 1 treatment again but stopped on day 8 due to disease progression. The other patient had her chemotherapy delayed by 2 weeks and the carboplatin dose was reduced to AUC 2 from AUC 2.5 before chemotherapy was recommenced.

Type of Chemotherapy	No. patients	of	Incidence neutropenia (CTC: 0.5-1 $\times$ 10 <sup>9</sup> )	G3 Incidence neutropenic sepsis	Incidence thrombocytopenia (CTC: $\geq$ 50 - $<$ 75 $\times$ 10 <sup>9</sup> )	G2 Incidence of G3/4 anaemia (CTC: $<$ 8g/dL)
wCP C (AUC 2 to 3) P 80-90 mg/m <sup>2</sup>	24		3 patients (5/179 inf) 2.8% of inf 12.5% of pts	0 patients (0/179 inf)	2 patients (3/179 inf) 1.8% of inf 8.3% of pts	0 patients (0/179 inf)
CwP C (AUC 6) q21d P 80 mg/m <sup>2</sup>	32		3 patients (3/407 inf) 0.7% of inf 9.3% of pts	1 patient (1/407 inf) 0.2% of inf 3% of pts	2 patients (3/407 inf) 0.7% of inf 6.2% of pts	12 incidences in 6 patients (12/407) 2.95% of inf

					18% of pts
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**Table 1:** Study population

<sup>a</sup> all in first line patients except one incidence in heavily pretreated patient (7th line)

<sup>b</sup> blood counts only done every three weeks (on day one) of each cycle, not weekly

No.: number, G: grade as per NCTC criteria, wCP: weekly carboplatin (C), and weekly paclitaxel (P), CwP: three weekly carboplatin (C) and weekly paclitaxel (P), AUC – area under the curve, inf- infusions, pts-patients

No lines chemotherapy	No pts wCP 24 (100%)	No pts CwP 32 (100%)
0	3 (13%)	27 (84%)
1-2	14 (58%)	4 (12.5%)
3-4	5 (21%)	0 (0%)
>4	2 (8%)	1 (3%)

**Table 2:** Number of lines of chemotherapy

No.: number, wCP: weekly carboplatin (C), and weekly paclitaxel (P), CwP: three weekly carboplatin (C) and weekly paclitaxel (P)

During 2010-2011, 32 patients received CwP, with blood tests scheduled only on the first day of each 21 day cycle. Although it could be argued that only the infusions when blood counts were taken should be compared, these two groups are only comparable by using the total number of infusions, whether or not a blood count was taken, as the blood counts taken at day 1 cannot tell us if there was neutropenia or thrombocytopenia later that cycle. 407 of 576 planned weekly infusions were delivered. The incidence of neutropenia was 12.5% (4/32). The neutropenic episodes occurred in 4 different individuals. In 2 of these patients the neutropenia was evident at day 1 of the 21 day cycle, on a scheduled blood count. Both these patients were being treated for relapse ovarian cancer and had received prior chemotherapy. The third patient with neutropenia had had day 8 of cycle 2 omitted because of diarrhoea and vomiting. An unscheduled blood count was taken, as part of this complaint, on day 15 and she

was found to be both neutropenic ( $0.6 \times 10^9$  L) and thrombocytopenic. Of these three patients who developed neutropenia one required a reduction in carboplatin dosing. The fourth patient had her final cycle of carboplatin weekly taxol delayed on day 1, because of neutrophils of 0.8 and was admitted febrile two days later. This was the only recorded case of neutropenic sepsis in the series. She received her final carboplatin two weeks late but the weekly paclitaxel was omitted.

Thrombocytopenia occurred in 2 patients (6.25%) including the aforementioned patient with concurrent neutropenia and thrombocytopenia at d15. A second patient had thrombocytopenia identified at day 1 of both cycles 2 and 3. Delays and dose reductions were made appropriately. In total 5 day 1 infusion were delayed due to haematological toxicity. There were 9 treatment delays due to non-haematological toxicity such as intercurrent infections, fatigue and stomatitis. Four patients had their dose of paclitaxel either reduced or stopped due to neuropathy. There were 12 incidences of G3-4 anaemia in 6 patients. Three patients required blood transfusion for symptomatic anaemia.

## Discussion

The success of weekly paclitaxel in patients with platinum resistant ovarian cancer has already resulted in a significant increase in the numbers of patients receiving weekly treatment as it is safe and well tolerated especially in those with limited treatment options. However it is time consuming especially if patients need to have blood tests performed and await the results on a weekly basis before chemotherapy is delivered. Given that many other tumour types are also beginning to explore and regularly use similar weekly paclitaxel regimens with varying success, the chemotherapy units themselves are also under considerable pressure and omission of the day 8 and 15 blood tests would simplify delivery. Publications about carboplatin and weekly taxol in ovary cancer to date concentrate on describing the response and progression free survival, simply documenting haematological toxicity. Tables 3 and 4 document these publications, showing the incidences of grade 3 and 4 anaemia, neutropenia and thrombocytopenia quoted.

Author (year)	No pts (no. inf)	Line of therapy	C dose (AUC)	P dose (mg/m <sup>2</sup> )	Threshold used X 10 <sup>9</sup>		Incidence per patients / no. infusions			
					Neutrophils	Plate-lets	G3-4 neutropenia	G3-4 thrombocytopenia	G3-4 anaemia	Febrile neutropenia
Sehouli (2002) [20]	21 (209)	1st line	2, 2.5, 3	100	2 × 10 <sup>9</sup>	100 × 10 <sup>9</sup>	24% pts 5.9% inf	24% pts 1.9% inf	0.9%	10% pts 1.3% inf
Katsumata (2001) [21]	(N/A)		2	80			61% pts		39%	
Havrilevsky (2002) [28]	29 (N/A)	Re-lapse	2	80	1.5 × 10 <sup>9</sup>	75 × 10 <sup>9</sup>	32% pts	14.2% pts	10%	3% pts
Dunton (2003) [29]	17 (N/A)		2	80			20% pts			

van der Burg (2012) [18]	108 (633)		4	90	1.0 × 10 <sup>9</sup>	50 × 10 <sup>9</sup>	51% pts 30% inf	29% pts 8% inf	20% pts 6% inf	2% pts 0.5% inf
Cadron (2007) [8]	29 (159)		4 q21d	90 q21d	1.0 × 10 <sup>9</sup>	100 × 10 <sup>9</sup>	94% pts 34% inf	25% pts 3% inf	24% pts 5% inf	13% pts 2% inf
Safra (2009) [30]	64 (N/A)		2	80	1.5 × 10 <sup>9</sup>	100 × 10 <sup>9</sup>	25% pts	0	0	1.6%
Sharma (2009) [19]	21 (N/A)	Rel-apse	3	70			34% pts	0	5% pts	10%
Cadron (2013) [31]	62 (828)		2.7	60	1.0 × 10 <sup>9</sup>	100 × 10 <sup>9</sup>	67% pts	35% pts	40% pts	6% pts
Hall (2013)	24 (179)	13% 1st line	2-3	80	1.0 × 10 <sup>9</sup>	100 × 10 <sup>9</sup>	12.5% pts 2.5% inf	8.3%pts 1.5% inf	?	3% pts 0.2% inf

**Table 3:** Details of publications showing treatment of ovarian cancer patients with weekly carboplatin and paclitaxel  
No. – number, G – grade as per NCTC criteria, wCP- weekly carboplatin (C), and weekly paclitaxel (P), CwP – three weekly carboplatin (C) and weekly paclitaxel (P), AUC – area under the curve, inf- infusions, pts-patients

Author (year)	No pts (no. inf)	1st line or relapse	C dose (AUC)	P dose (mg/m <sup>2</sup> )	Threshold used		Incidence per patients / no. infusions			
					Neutrophils	Plate-lets	G3-4 neutropenia	G3-4 thrombocytopenia	G3-4 anaemia	Febrile neutropenia
Rose (2005) [17]	28 (186)	Re-lapse	5	80 (but 89% pts reduced to 60)	1.5 × 10 <sup>9</sup>	100 × 10 <sup>9</sup>	53% of pts (8% of inf)	17% of pts (2.6% of inf)	10% of pts (2% of inf)	3% of pts (<1% of inf)
Hoekstra (2009) [24]	20	Re-lapse	5	80	1.5 × 10 <sup>9</sup>	75 × 10 <sup>9</sup>	35% of pts	0	0	10%
Katsumata (2009) [9]	314	1st line	5	80	0.5 × 10 <sup>9</sup> wkly	50 × 10 <sup>9</sup> wkly	92% of pts	44% of pts	69% of pts	9%
Lortholary (2011) [25]	51	Re-lapse	5	80	1.5 × 10 <sup>9</sup>	100 × 10 <sup>9</sup>	54% of pts	4% of pts	19% of pts	4%
Hall (2013)	32 (407)	81% 1st line	6-May	80	1.0 × 10 <sup>9</sup> on d1	100 × 10 <sup>9</sup> on d1	9.3% of ptsa 0.6% inf	6.2% of ptsa 0.6% inf	N/A	3% of pts

**Table 4:** Details of publications showing treatment of ovarian cancer patients with 3-4 weekly carboplatin and weekly paclitaxel

No. - number, G - grade as per NCTC criteria, wCP - weekly carboplatin (C), and weekly paclitaxel (P), CwP - three weekly carboplatin (C) and weekly paclitaxel (P), AUC - area under the curve, inf- infusions, pts-patients

From Table 3, it can be seen that amongst patients receiving weekly carboplatin and weekly paclitaxel the incidence of neutropenia ranges from 2.5% to 67%. Although many factors such as ethnicity, nutritional status, and lifestyle can be implicated for this variation, the difference in the denominator reported (number of infusions versus number of patients) is most likely to be the main cause. In respect to weekly therapy, some publications report incidences of haematological toxicity in relation to the total number of patients and others in relation to the number of infusions delivered. For example, thrombocytopenia in this population is reported as ranging from 1.9% (infusions delivered) to 51% (of patients). All parameters quite obviously also relate to the number of times blood counts are taken; if taken every week then expected nadirs are regularly identified. As might be expected, van der Burg 2012, detail identical incidences of G3/4 neutropenia and thrombocytopenia per patient receiving weekly

chemotherapy compared with a significant cohort of the same patients changing to 3 weekly carboplatin/paclitaxel after 6 weeks [18].

The most important measure of haematological toxicity is febrile neutropenia which reportedly ranges from 0-10% in this group of patients and is considered acceptable in patients with advanced disease undergoing intensive chemotherapy. Sharma et al report the highest incidence of persistent neutropenia, with significant dose delays (38% due to neutropenia) and an incidence of febrile neutropenia of 10% (2/20) including 1 death from neutropenic sepsis [19]. The weekly doses used however carboplatin AUC 3 and paclitaxel 70 mg were/m<sup>2</sup>; one patient in our series was treated with the same dose of carboplatin AUC3 and similarly persistent neutropenia was noted. It has now been established that the safest and most pragmatic dose of carboplatin to be used weekly is an AUC of 2.0 or 2.5 and the optimal dose of weekly paclitaxel given for relapsed ovarian cancer ranges between 70 and 100 mg/m<sup>2</sup>, the most popular being 80 mg/m<sup>2</sup> weekly [20-22].

Table 3 also sets out (from the Methods sections) the variance of acceptable levels of neutrophils and platelets for treatment to go ahead. This ranges from >1.0 × 10<sup>9</sup> to >2.0 × 10<sup>9</sup> neutrophils weekly and >1.0 × 10<sup>9</sup> to >3.0 × 10<sup>9</sup> on day 1 of a three - four weekly cycle. For

platelets, the range is  $>50 \times 10^9$  to  $>100 \times 10^9$  weekly or  $>75 \times 10^9$  to  $>100 \times 10^9$  on day 1 of a three to four weekly cycle. Interestingly there is no obvious relation between the thresholds for treatment and incidence of neutropenia (including febrile) or thrombocytopenia, although there is a suggestion that the lower the threshold accepted for treatment the higher the incidence of anaemia.

For patients receiving weekly paclitaxel in combination with standard three or four weekly carboplatin, the incidences of haematological toxicity are predictably different. The question is whether the weekly paclitaxel adversely impacts on the expected haematological toxicity of the carboplatin delivered, increasing the risks of clinically significant febrile neutropenia and other complications. Three weekly carboplatin and weekly paclitaxel chemotherapy was the experimental arm of a Japanese trial examining the first line treatment of stage II-IV ovarian cancer patients. Katsumata et al. randomised 637 patients to receive either CwP or carboplatin and paclitaxel given conventionally, every 3 weeks (3wCP). This study demonstrated that patients who received CwP had a longer median progression free survival at 3 years (28 versus 17.2 months) and a recent oral presentation confirmed a 7.6% higher overall survival at 6 years in the CwP group (58.6% vs. 51% 5 y OS) [23]. There was only a minimal increase in toxicity reported in the dose dense arm. The UK ICON8 trial is currently recruiting similar first-line patients to a three-arm trial to corroborate and investigate further the impact of scheduling carboplatin and paclitaxel. Much can be learnt from the women included in the JGOG 3016 trial, although it is important to remember that these patients are all chemo naïve.

Sensible dose reductions, such as we might all use in practice, were built into the JGOG 3016 trial schema, the carboplatin dose was reduced when febrile neutropenia occurred, or an absolute neutrophil count less than  $0.5 \times 10^9$  cells per L persisted for 7 days or more. The carboplatin dose was also reduced if either the platelet count was less than  $10 \times 10^9$  per L, or between  $10 \times 10^9$  per L and  $50 \times 10^9$  per L with bleeding tendencies, or the treatment was delayed for any haematological toxicity for more than 1 week. As in our practice, GCSF was not available routinely but, unlike our practice, was used in 187 (60%) patients assigned to the dose-dense regimen and in 214 (67%) assigned to the conventional regimen. Despite this, haematological toxicity was the most common cause for the discontinuation of treatment: 68 [60%] of 113 patients assigned to the dose-dense regimen vs. 30 [43%] of 69 assigned to the conventional regimen;  $p=0.03$ . The incidence of neutropenia, thrombocytopenia and anaemia were all higher in those having dose dense chemotherapy compared with the conventional regimen, 92%, 44% and 69% versus 88%, 38% and 44% respectively. But these differences are not large or significant, except perhaps anaemia. Most importantly, the incidence of febrile neutropenic episodes were identical in both arms, 9%. Our series of patients is most like the JGOG 3016 population given that the majorities were receiving first line therapy. Five of our patients were being treated for relapsed ovarian cancer with CwP.

An increasing number of studies demonstrate that the use of three weekly carboplatin and dose dense paclitaxel (CwP) in recurrent ovarian cancer also results in favourable response rates and an acceptable toxicity profile [17,24,25]. A phase 1 dose finding study suggested that doses above carboplatin AUC 5 and weekly paclitaxel  $80 \text{ mg/m}^2$  are eventually limited by haematological toxicity (febrile neutropenia and thrombocytopenia, after 6-9 weeks of therapy) [26]. All four studies described in Table 4, other than this one, detail treatment doses starting at carboplatin at an AUC of 5 and paclitaxel

weekly at a dose of  $80 \text{ mg/m}^2$ . The incidence of grade 3-4 neutropenia ranges from 35-54% and grade 3-4 thrombocytopenia, 0-17.8% and grade 3-4 anaemia 0-19%. Febrile neutropenia was reported with an incidence of up to 10%. Most relapsed patient studies describe treatment on a 28 day cycle which might have given sufficient time for the bone marrow to recover, explaining the lower incidence in relapsed patients in comparison to the patients on a 21 day cycle in Katsumata 2009 [9]. In our 21 d cycle series, 2 of the CwP patients were neutropenic at day 1 of the 21 day cycle and their chemotherapy delayed and doses adjusted in line with normal practice. The third patient with neutropenia in our series had had day 8 of cycle 2 omitted because of diarrhoea and vomiting. Blood parameters were rechecked as a consequence of her general condition and doses altered accordingly.

A criticism of this review is that it is inaccurate to compare our groups as in the CwP group where blood counts are only done every three weeks (on Day 1) the expected neutrophil and platelet nadir counts are missed. However it is established practice in this group of patients receiving three weekly treatment not to routinely measure nadir counts which our comparison now shows is also feasible in patients treated weekly. The same may not be true for other tumour types weekly paclitaxel is used to treat breast cancer in both the adjuvant and metastatic settings. Sparano et al. compared docetaxel and paclitaxel regimens adjuvantly given weekly and 3 weekly in breast cancer patients [27]. They reported that weekly paclitaxel improved disease free and overall survival compared to paclitaxel given every 3 weeks when given after doxorubicin and cyclophosphamide. The incidence of febrile neutropenia was low in patients treated with both weekly paclitaxel and 3 weekly paclitaxel 1% ( $n=1231$ ) and  $<1\%$  ( $n=1253$ ) respectively. Seidman et al. evaluated the efficacy of weekly paclitaxel compared to 3 weekly paclitaxel with trastuzumab in metastatic breast cancer. Patients receiving weekly paclitaxel and trastuzumab had improved response rates and time to progression. The incidence of febrile neutropenia was low in both groups being 4% and 3% in those receiving 3 weekly or weekly paclitaxel respectively. However, in both these studies patients were allowed to receive granulocyte colony stimulating factors for severe neutropenia as well as neutropenic sepsis. Although the findings from our study suggest that blood counts on day 8 and 15 can be omitted in medically well gynaecological cancer patients, this is not necessarily applicable to all malignancies. Patients with metastatic breast cancer for example may have an increased likelihood of bone marrow involvement exacerbating the likelihood of any myelosuppression caused by chemotherapy.

Another potential disadvantage for omitting the weekly blood counts is that this might result in more delays in treatment delivery. There is no evidence from this retrospective review that, even in the pretreated patient group (wCP), omitting blood counts resulted in significantly different incidences of delay. Asymptomatic neutropenia/thrombocytopenia is only likely to go undetected for a maximum of 2 weeks (assuming the nadir occurs at 10-14 days) as day 1 blood tests are still performed. Given that the overall doses of the cytotoxic agents are similar over the three week period of each cycle, it is unlikely that there will be any more delays for patients receiving three weekly versus weekly therapy, in fact it could be argued that regularly doing weekly blood tests might result in unnecessary treatment delays by identifying and acting on 'expected' nadirs. A prospective study would be the best way to determine this point accurately [28-31].

## Conclusion

The findings from our study suggest that gynaecological cancer patients receiving entirely weekly regimens in the form of wCP, whether in first-line or relapse, have a low incidence of neutropenia and thrombocytopenia and it is safe to omit the d8 and d15 blood test routinely. Treatment with CwP causes a significantly higher incidence of neutropenia and thrombocytopenia but does not lead to any significant increase of clinical complications such as febrile neutropenia when used in patients who are chemo naïve and omission of routine blood count analyses on day 8 and 15 is acceptable. In pretreated patients with relapsed ovarian cancer, treatment with CwP is more problematic as patients are more frequently delayed for many different reasons. Provided patients are well enough on medical review, delivery of weekly chemotherapy can proceed without weekly blood counts, although it remains obligatory to check these at the first day of each 3 or 4 weekly cycle.

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