JOURNAL OF ONCOLOGY PHARMACY PRACTICE

Original Article

J Oncol Pharm Practice
0(0) 1–7

DOI: 10.1177/1078155218796912
journals.sagepub.com/home/opp
SAGE

Variability of carboplatin dose calculation methods in Spain

Cristina Cuesta Grueso[1], Amparo Burgos San José[2], Gerardo Cajaraville Ordoñana[3], Jaime E. Poquet Jornet[1], Irene Mangues Bafalluy[4] and María S. Díaz Carrasco[5]

Abstract

Objective: To describe and analyze the variability in carboplatin dosing strategies in Spanish hospitals.

Methods: We designed a questionnaire consisting of 19 multiple-choice items structured in two sections (hospital characteristics and carboplatin dosing data). The questionnaire was sent by e-mail to all the oncology pharmacists included in the register of the Spanish Oncology Pharmacy Group (GEDEFO), and we analyzed the completed questionnaires.

Results: Response rate was 33.5% from a total of 185 pharmacy services invited to take part in the survey. All hospitals used the Calvert formula to calculate carboplatin dose with glomerular filtration rate estimated by a formula, most commonly the Cockcroft-Gault equation (80.7%). Carboplatin doses were capped in most hospitals (91.9%): 54.8% capped creatinine clearance at 125 mL/min, 11.3% capped serum creatinine, and 19.3% capped both creatinine clearance and serum creatinine. Serum creatinine cut-off values ranged from 0.36 mg/dL to 1 mg/dL. The most commonly used body weight was actual body weight for underweight, normal weight, and overweight patients. The use of adjusted ideal body weight increased in obese and especially in morbidly obese patients.

Conclusion: The results from this survey show the variability that exists in carboplatin dose calculation methods among Spanish hospitals and the need to continue investigating to find the optimum dose calculation method and unify criteria to avoid differences between sites that can affect effectiveness and toxicity of carboplatin-containing treatments.

Keywords

Carboplatin, survey, dosing adjustments, obese, overweight

Date received: 23 March 2018; revised: 30 July 2018; accepted: 4 August 2018

Introduction

Intravenous carboplatin dose can be calculated by body surface area (BSA) like other chemotherapy drugs.[1] However, since carboplatin is predominantly subject to renal clearance and given the relationship between the area under the plasma carboplatin concentration–time curve (AUC) of free platinum and the degree of thrombocytopenia and neutropenia, it is advisable to use dosing formulas based on both renal function and AUC.[1]

The most widely used formula in clinical practice is the Calvert equation which was validated based on the isotopic measurement of glomerular filtration rate (GFR) using ^{51}Cr-EDTA. However, this method is costly and not easily available, and therefore not commonly used in clinical practice. GFR can be estimated using creatinine clearance (CrCl) which can be

[1]Pharmacy Department, Hospital of Denia Marina Salud, Alicante, Spain
[2]Pharmacy Department, Hospital General Universitario de Alicante, Alicante, Spain
[3]Pharmacy Department, Fundación Onkologikoa, San Sebastián, Spain
[4]Pharmacy Department, Hospital Universitari Arnau de Vilanova de Lleida, Lleida Spain
[5]Pharmacy Deparment, University Hospital Virgen de la Arrixaca, Murcia, Spain

Corresponding author:
Cristina Cuesta Grueso, Department of Hospital Pharmacy, Hospital de Denia (Marina Salud), Partida Beniadlà sn, 03700 Denia, Alicante, Spain.
Email: cris.cuesta34@gmail.com

determined from a 24-h urine collection, but the preferred methods used for CrCl estimation are formulas such as the Cockcroft-Gault (CG), Jelliffe, Wright, modification of diet in renal disease (MDRD), and Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations.[2–6] Nevertheless, CrCl values obtained with these formulas vary and some use body weight despite the controversy regarding which values should be used (actual body weight (ABW), ideal body weight (IBW) or adjusted ideal body weight (AIBW)), especially for extreme values.

Furthermore, these formulas use the serum creatinine (sCr) value which is not only dependent on renal function but also on muscle mass, diet, hydration status, and non-renal excretion. Also, the sCr measurement method currently used in clinical laboratories is calibrated against a standard (IDMS) and thereby produces values that differ from the ones that were used when certain of these GFR estimation formulas were developed. In general, the current method gives lower sCr values, which can lead to overestimations of creatinine clearance and therefore overdosing of carboplatin. Several groups and institutions have put forward measures to minimize this risk – such as the FDA who proposes a maximum dose strategy[7] – and different recommendations exist for a minimum sCr value (around 0.6–0.8 mg/dL) when estimating GFR in patients with abnormally low sCr.[7–9]

Thus, dose calculation based on sCr values is subject to multiple variables (formula chosen, weight used, creatinine measurement technique, endogenous production, etc.) and the dose obtained for a single patient in different settings may vary and have clinical repercussions.

Aim of the study

The objective of this study was to describe and analyze the variability in carboplatin dosing strategies in Spanish hospitals.

Ethical approval

According to the Spanish law, no ethical approval was required for this study.

Methods

In October 2015, a survey designed by two oncology pharmacists was approved by the executive committee of the Spanish Oncology Pharmacy Group (GEDEFO), a consolidated group of hospital pharmacists who work to improve the quality of oncology–hematology care.

In November 2015, the questionnaire was sent by e-mail together with a letter explaining the objective of the study and requesting participation from all the oncology pharmacists included in GEDEFO's register. A reminder was sent four weeks later, with a deadline to return the completed questionnaires by 15 December 2015.

Each pharmacy service could only send back one survey form.

Description of the questionnaire

The questionnaire was structured in two main sections, each divided into different parts consisting of various items:

- Section 1: Hospital data
  - Part 1: Hospital characteristics: general, oncological, university or regional; public, private or privately managed public hospital, and number of beds.
  - Part 2: Daily activity of the oncology–hematology unit of the pharmacy service, number of pharmacists working in the unit and their specific training.
  - Part 3: Training provided by the pharmacy service.
- Section 2: Carboplatin dosing data. This section included all the questions related to the carboplatin dosage methods:
  - Part 1: Items related to the prescription-validation process.
  - Part 2: Items related to formulas used to calculate the dose of carboplatin and variables included:
    - ☐ Formula for carboplatin dosage: Calvert, Chatelut, Bénézet, or other options.
    - ☐ If the Calvert formula was selected: Method for measuring or estimating CrCl (CG, Jelliffe, Wright, MDRD, CKD-EPI, or other) and carboplatin dose capping (maximum CrCl, minimum sCr, or other).

Overall, the questionnaire consisted of 19 multiple-choice items.

Some items had an "other (specify)" option to allow for free text entry if none of the predefined answers provided were an option for certain pharmacy services. In these cases, we reviewed all the free-text answers in order to ensure they were not conceptually similar to any of the options provided in the questionnaire. If we considered they were similar, we included them in one of the predefined options.

Results

Sixty-two questionnaires were received from the 185 pharmacy services we had invited to take part in the survey (response rate 33.5%).

Table 1. Characteristics of respondent hospitals (n = 62).

	n (%)
Scope of hospital services	
General	19 (30.7)
Oncological	2 (3.2)
University	24 (38.7)
Regional	15 (24.2)
Other	2 (3.2)
Type of management	
Public	48 (77.4)
Private	5 (8.1)
Privately managed public hospital	8 (12.9)
Other	1 (1.6)
Number of beds	
Less than 200	14 (22.6)
Between 200 and 499	21 (33.9)
Between 500 and 999	19 (30.6)
1000 or more	7 (11.3)
Not described	1 (1.6)

Hospital data

Hospital characteristics are shown in Table 1. The mean number of chemotherapy doses prepared per month was 1498 (SD: ±1050). The number of pharmacists per oncology–hematology unit in the pharmacy services is shown in Table 2. Of the participating hospitals, 66.1% had one pharmacist and the rest had two or more, resulting in a total of 95 pharmacists in the oncology–hematology units in the pharmacy services overall.

Apart from the training received in a hospital to qualify as a hospital pharmacist, 48 hospitals (77.4%) reported having pharmacists with specific additional training which consisted of:

- Board Certified Oncology Pharmacist program of the Board of Pharmacy Specialties, American Pharmacists Association (47 hospital pharmacists, 49.5% of all pharmacists in the oncology–hematology units)
- Master's degree in Oncology Pharmacy. University of Valencia (Spain) (24 hospital pharmacists, 25.3%)
- Other specific training (five hospital pharmacists, 5.3%)

Most hospitals (91.3%) reported having training programs consisting of: Supervised practice for a Pharmacy Degree (88.7% of all hospitals), a four-year training program for pharmacists to become hospital pharmacists (67.7%), and training programs for pharmacy technicians (30.6%).

Table 2. Pharmacists in the oncology–hematology unit.

	N (%)	Total pharmacists
1	41 (66.1)[a]	41
2	11 (17.8)[b]	22
3 or more	10 (16.1)[c]	32
Total	62	95

[a]Twenty-two (53.7) hospitals with one full time pharmacist; 19 (46.3) with one part time pharmacist.
[b]Seven (63.6) with two full time pharmacists; one (9.1) with two part time pharmacists; three hospitals (27.3) with one part time pharmacist and one full time pharmacist.
[c]Six (60.0) hospitals with full time pharmacists; four (40.0) hospitals with part time and full time pharmacists.

Carboplatin dosing data

In 91.9% of cases, physicians calculated the carboplatin doses and pharmacists validated them. Only four hospitals (6.5%) reported that carboplatin doses were calculated by pharmacists and one reported that pharmacists did not validate carboplatin doses prescribed by physicians.

The most common way of prescribing was via electronic prescription software (53 hospitals, representing 85.5% of all cases). Specifically, 52 hospitals recorded prescriptions in an electronic prescription database (integrated with medical records in 12 hospitals) and one recorded prescriptions directly in the medical records. Manual prescription was reported by nine hospitals (14.5%).

Overall, the hospitals used 11 different software/databases: Farmis-Oncofarm® was the most commonly used one (44.2%) followed by Oracle® (15.4%), and FarmaTools®, SISinf®, and the hospitals' own software were used in the same proportion (5.8%).

As for the recommendations made by the pharmacists when validating carboplatin doses, 57 hospitals (91.9%) reported that physicians usually accepted the recommendations. Three hospitals (4.8%) gave other answers indicating, for example, that recommendations were occasionally accepted or that the question was not applicable because no carboplatin dose validation was performed by pharmacists. Only two hospitals (3.2%) reported that the pharmacists' suggestions were not accepted. With regard to the method used to calculate carboplatin dose, 88.7% of hospitals reported a physician–pharmacist consensus method (Table 3) which, in all cases, included the Calvert formula. No hospital reported the use of other formulas such as Chatelut or Bénézet.

GFR used in the Calvert equation was estimated using a formula in 100% of hospitals. Ten hospitals also determined CrCl from a 24-h urine collection in some patients, such as geriatric patients or patients with

Table 3. Carboplatin dosing data (n = 62).

	n (%)
Consensus method physician–pharmacist for carboplatin dosing	
Yes	55 (88.7)
No	7 (11.3)
Formula for carboplatin dosage	
Calvert	62 (100.0)
Estimation of GFR in Calvert formula	
Estimation of CrCl by a formula	52 (83.9)
Generally CrCl by a formula and from 24-h urine for some patients	10 (16.1)
Equation for CrCl estimation in the Calvert formula	
Cockcroft-Gault	50 (80.7)
MDRD	7 (11.3)
CKD-EPI	3 (4.8)
Cockcroft-Gault and another formula	2 (3.2)
Capping parameters in the equation for CrCl estimation in the Calvert formula	
Maximum CrCl only	34 (54.8)
Maximum CrCl and minimum sCr	12 (19.3)
Minimum sCr only	7 (11.3)
No capping values	5 (8.1)
Other	4 (6.5)
Dose adjustment in special population	
Geriatric patients	12 (19.4)
Cachectic patients	17 (27.4)
Amputees	12 (19.4)

MDRD: modification of diet in renal disease; CrCl: creatinine clearance; sCr: serum creatinine; CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration; GFR: glomerular filtration rate.

germ-cell tumors. No hospital reported the use of measured GFR by ^{51}Cr-EDTA clearance.

Fifty hospitals (80.7%) used the CG formula as the only option to estimate CrCl. Two hospitals also selected the Jelliffe and MDRD equations, respectively. The other hospitals only used MDRD or CKD-EPI.

Overall, carboplatin dose capping occurred in 91.9% of hospitals: CrCl was capped at 125 mL/min in 54.8% of hospitals; sCr was capped in 11.3%; and both CrCl and sCr were capped in 19.3% (Table 3). Altogether, 19 hospitals applied carboplatin dose capping using sCr cut-off values (either sCr only or both sCr and CrCl). The cut-off values for sCr differed: six hospitals used a minimum sCr of 0.6 mg/dL; four hospitals used a minimum of 0.7 mg/dL; and the other hospitals each used 1 mg/dL, 0.67 mg/dL, 0.65 mg/dL, 0.5 mg/dL, 0.4 mg/dL, 0.36 mg/dL, 0.6–0.7 mg/dL, or 0.5 mg/dL for women and 0.7 mg/dL for men. No hospital reported the use of formulas that included cystatin C value.

The results regarding the type of body weight employed in the CG formula (the only formula for estimating CrCl that includes body weight as a variable) are shown in Figure 1. The most commonly used type of body weight was ABW for underweight, normal weight, and overweight patients. For obese and morbidly obese patients, IBW and AIBW were more important. In fact, 50% of hospitals employed AIBW in morbidly obese patients.

Discussion

The methods and criteria used for carboplatin dosing vary, as there is no universally accepted standard and this leads to many controversies.[7,8,10–17] This study's main contribution is that it shows the existing variability in carboplatin dosing in clinical practice in Spain.

We would like to highlight the fact that the hospitals that participated in the survey were mainly public hospitals, both general and university hospitals, and represented a large sample of this type of institutions. It is also of note that in most cases there was only one pharmacist involved in chemotherapy drug dosing despite the complexity of the activity and that these pharmacists were highly trained.

As for carboplatin dosing, the first remarkable positive aspect revealed by the survey is the high degree of physician–pharmacist consensus.

The Calvert formula, which was used by 100% of the respondent hospitals to estimate the dose of carboplatin, was undoubtedly the most widely used formula overall. Other formulas such as the Chatelut[18] or Bénézet[19] equations have not been widely implemented in clinical practice. According to a survey conducted in 2010 by the Hematology Oncology Pharmacy Association[20] (HOPA), the most extensively used formula in the United States (US) is the Calvert formula. The British Oncology Pharmacy Association (BOPA) also recommends using this dose calculation method in its verification guidelines.[12]

The Calvert equation was validated based on the isotopic measurement of GFR using ^{51}Cr-EDTA, but this method is costly and not easily available. GFR can be estimated using CrCl which can be determined from a 24-h urine collection. However, the survey shows that this method is rarely used and that CrCl is usually calculated from sCr data using estimation formulas even though the 24-h collection method may be preferable, especially in populations with altered muscle mass, body mass index (BMI) below 19 or above 35, elderly patients, etc.[21,22]

According to the survey, the most common estimation formula is the CG equation which is the one typically used for dosing of drugs with renal excretion in general and for carboplatin in particular. It is also the most commonly used formula in the US (89.3%), as shown in the HOPA survey.[20] The Gynecologic Oncology Group (GOG), which previously utilized the Jelliffe formula in its studies, currently also recommends

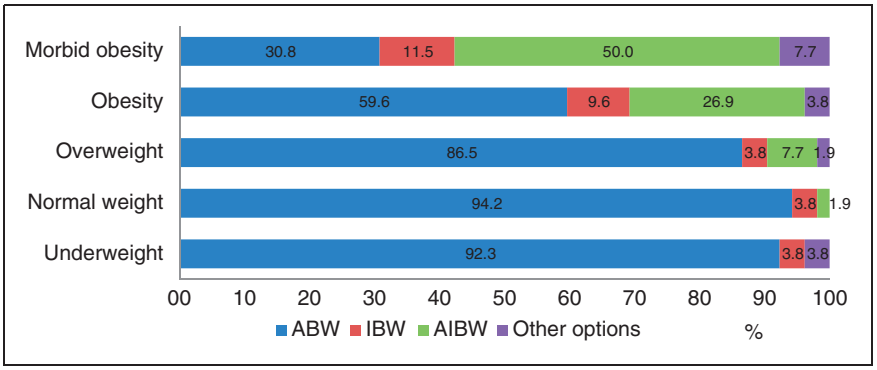

Figure 1. Body weight employed in the Cockcroft–Gault formula (n = 45).
ABW: actual body weight; IBW: ideal body weight; AIBW: adjusted ideal body weight.

the use of CG.[15] However, BOPA recommends using the Wright formula,[6] developed from a population of oncology patients. This formula has been evaluated in different studies with variable results[9,23,24] and its use has not been widely implemented. It also has the disadvantage that there is less experience with it in special populations such as obese or elderly patients.

Nephrology associations currently include the MDRD and CKD-EPI equations (designed for the diagnosis and classification of kidney disease) in their guidelines on drug dosing.[13] Several studies report that carboplatin dosage adjustments determined by these two equations result in similar or better adjustments compared to the use of CG.[25–28] Nevertheless, other studies describe worse adjustments[23,29] with these formulas, mainly in special populations (e.g. elderly patients). In general, no single formula has proven to be clearly superior to CG in every context.

The survey results also highlight that 91.9% of the sites use dose capping, mostly by using a maximum CrCl value based, when estimated, on the Food and Drug Administration[7] and America Society of Clinical Oncology[11] recommendations. The use of a minimum sCr value for these calculations is less common and cut-off values greatly differ. In the HOPA survey, 55% of the sites performed adjustments for values ranging from 0.7 to 1 mg/dL.

It is important to establish a minimum sCr value provided the estimation formulas used have not been re-expressed with current methods for measuring creatinine, as is the case with CG. At present, certified laboratories use IDMS-standardized methods, producing values that are lower than former non-IDMS values. Using such values in classical formulas overestimates CrCl, leading to a risk of carboplatin overdosing. No unambiguous specific cut-off value has been established either. The NCI recommends minimum values of 0.6 mg/dL,[14] while the GOG group has established a minimum of 0.7 mg/dL.[15]

Given the predominant use of CG, it should be emphasized that this formula was developed using patients' ABW, but in a population in which overweight or obese patients were not adequately represented. Thus, the use of ABW for this population is debatable. Various weight descriptors have been studied based on patient BMI, but results have been heterogeneous.

For low-weight patients (BMI<18.5), the survey shows that ABW was the most widely used descriptor. This is an option supported by the study by Winter et al.[17] which showed that adjustment was improved when CrCl was estimated in this population using this weight descriptor. However, other authors have obtained better adjustments using AIBW[16] or lean body mass.[10]

The main descriptor in normal-weight patients was ABW, but IBW – as supported by the results of the study by Winter et al.[17] – and AIBW – as recommended by Kaag et al.[16] – were also used, albeit in a minority of cases. The GOG group recommends using ABW for a BMI<25.

In overweight and obese patients, the use of other descriptors, mainly AIBW, progressively increases in parallel with BMI. Various studies have shown a better dose adjustment in obese patients when CrCl[17,18,24,25,30] or carboplatin clearance estimations were based on AIBW.[8,10,16]

The advantage of using AIBW versus ABW for carboplatin dose calculation in cases of overweight is not clear either,[24,30] although it is the descriptor that obtained the best adjustment in several studies,[8,10,16] especially when BMI>27. Currently, the GOG group recommends using this weight descriptor starting at a BMI of 25 kg/m.[25] However, in 2012, the ASCO recommended administering full doses of cytotoxic drugs based on ABW in overweight and obese patients, although at the same time, it also advised adopting the FDA's recommendation on carboplatin maximum dose.[7]

The HOPA survey[20] shows that the use of AIBW is more common in US hospitals than in Spanish ones (46.5%). Nonetheless, the comparison of the results of this survey with those of the survey performed by Anglada et al., in which only 12% of participating hospitals used AIBW to estimate CrCl in obese patients,[31] shows that its use is increasing in Spain.

Although the percentage of use of IBW in overweight or obese patients is low, it is still noteworthy. In studies in which this weight descriptor has been evaluated, it clearly underestimates CrCl.[17,24,32]

Janowitz et al.[28] recently published a new glomerular filtration rate estimation model based on a population of 2470 cancer patients. The authors show that better estimation results are obtained with their model compared to classical models. In addition, among the standard former models, they identify the patient BSA-adjusted CKD-EPI as the best estimation method. However, despite its methodological robustness, this study fails to specify certain aspects: (1) whether the sCr determination methods used were IDMS-standardized, (2) what weight descriptors were used in the CG formula, and (3) whether minimum sCr or maximum estimated CrCl values were capped. As mentioned above, these factors clearly affect the results and their accuracy can improve estimations in different clinical situations.

The different estimation methods, different CrCl and minimum sCr capping values, and different weights used in the CG formula can lead to major differences in the calculated carboplatin dose. Although these differences may theoretically result in differences in the effectiveness or toxicity of carboplatin-containing chemotherapy regimens, a conclusive correlation cannot be established for lack of data or studies that prove it.

Conclusion

The results from this survey show the variability that exists in carboplatin dose calculation methods among Spanish hospitals and the need to continue investigating to find the optimum method and unify criteria to avoid differences between sites that can theoretically affect effectiveness and toxicity of carboplatin-containing treatments.

Acknowledgments

The following pharmacists have participated in this study: Teresa Calleja (La Coruña), Juan Francisco Marín (Jaén), Dolores Camacho (Alicante), Ángel Albacete (Sevilla), Bárbara Boyeras (Palma de Mallorca), Sonia González (Vigo), Tomás Arrazola (Marbella), Rocío Romero (Mahón), Mónica Carbajales (Gijón), Esther Carcelero (Barcelona), David Conde (Barcelona), Maruxa Hernández (Barcelona), Gerardo Cajaraville (San Sebastián), Eva Gonzalez (Santa Coloma de Gramanet), Mª Ángeles López-Montenegro (Játiva), Mariana Zaragoza (Ronda), Montserrat Rey (Hospitalet de Llobregat), Margarita Nigorra (Palma de Mallorca), Maria Sacramento Díaz (Murcia), Ana Aguirrezabal (Bilbao), Mònica Calonge (Mollet del Vallés), Araceli Iglesias (Lugo), Silvia Artacho (Sevilla), Carmela Borrell y Asunción Albert (Valencia), Alba Manzaneque (Terrassa), María Angeles Faraldo (Orense), Beatriz Bernárdez (Santiago de Compostela), Raúl Diez (Getafe), Marta Manso (Majadahonda), Laura Delgado (Coslada), Antonia Planas (Manresa), Maria del Carmen Martinez (Puerto Real), María José Martínez (Cádiz), Mar Montes (Barcelona), María José Agustín (Zaragoza), Margarita Garrido (Marbella), Estela Moreno (Barcelona), Eva González-Haba (Madrid), Diana Pérez (Alcalá de Henares), Mónica Martínez (Cartagena), Nuria Pi (Barcelona), Ana Rosa Rubio (Toledo), Eva Castillo (Madrid), Celia Abajo (Valladolid), Piedad Toro (Alcorcón), Cristina Cuesta (Denia), Javier Letéllez (Fuenlabrada), Mª Amparo Lucena (Leganés), Maria-Josep Carreras (Barcelona), Susana Redondo (Terrassa), Amparo Burgos (Alicante), Ana María Moreno (Aranda de Duero), Inmaculada Jiménez (Elche), Belen Matilla (León), José Antonio Marcos (Sevilla), David López (Badalona), Francesc Soler (Girona), Yolanda Calafell (Sant Pere de Ribes), Virginia Gol (Figueres), Nieves Muro (Badalona), María Isabel Magaña (Palamós), Berta Gracia (Sant Joan Despí).

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Cristina Cuesta Grueso http://orcid.org/0000-0002-2402-3042

References

1. American Society of Health-System Pharmacists. *Drug information*. Bethesda, MD: Author, 2012.
2. Cockcroft DW and Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976; 16: 31–41.
3. Jelliffe RW. Letter: creatinine clearance: bedside estimate. *Ann Intern Med* 1973; 79: 604–605.
4. Levey AS, Stevens LA, Schmid CH, et al.; CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009; 150: 604–612.
5. Levey AS, Bosch JP, Lewis JB, et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. MDRD (Modification of Diet in Renal Disease Study Group). *Ann Intern Med* 1999; 130: 461–470.

6. Wright JG, Boddy AV, Highely M, et al. Estimation of glomerular filtration rate in cancer patients. *Br J Cancer* 2001; 84: 452–459.
7. FDA Food and Drug Administration (FDA). Carboplatin dosing, www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm228974.htm (accessed 17 August 2018).
8. Herrington JD, Tran HT and Riggs MW. Prospective evaluation of carboplatin AUC dosing in patients with a BMI>or=27 or cachexia. *Cancer Chemother Pharmacol* 2006; 57: 241–247.
9. Dooley MJ, Poole SG, Rischin D, et al. Carboplatin dosing: gender bias and inaccurate estimates of glomerular filtration rate. *Eur J Cancer* 2002; 38: 44–51.
10. Ekhart C, Rodenhuis S, Schellens JH, et al. Carboplatin dosing in overweight and obese patients with normal renal function, does weight matter? *Cancer Chemother Pharmacol* 2009; 64: 115–122.
11. Griggs JJ, Mangu PB, Anderson H, et al.; American Society of Clinical Oncology. Appropriate chemotherapy dosing for obese adult patients with cáncer: American Society of Clinical Oncology clinical practice guideline. *J Oncol* 2012; 30: 1553–1561.
12. British Oncology Pharmacy Association. Guidance to Support BOPA Standards for Clinical Pharmacy Verification of Prescriptions for Cancer Medicines. v1.5, www.bopawebsite.org/publications/guidelines-standards (accessed 17 August 2018).
13. National Kidney Disease Education Program: CKD and drug dosing: information for providers, www.niddk.nih.gov/health-information/health-communication-programs/nkdep/a-z/ckd-drug-dosing/Pages/CKD-drug-dosing.aspx (accessed 17 August 2018).
14. Cancer Therapy Evaluation Program. Follow-up for information letter regarding AUC-Based dosing of carboplatin, https://ctep.cáncer.gov/content/docs/carboplatin_information_letter.pdf (2010, accessed 17 August 2018).
15. Roisin O'Cearbhaill. Special report. New Guidelines for Carboplatin Dosing. Newsletter Gynecologic Oncology Group, www.gog.org/Spring2012newsletter.pdf (2012, accessed 17 August 2018).
16. Kaag D. Carboplatin dose calculation in lung cancer patients with low serum creatinine concentrations using CKD-EPI and Cockcroft–Gault with different weight descriptors. *Lung Cancer* 2013; 79: 54–58.
17. Winter MA, Guhr KN and Berg GM. Impact of various body weights and serum creatinine concentrations on the bias and accuracy of the Cockcroft-Gault equation. *Pharmacotherapy* 2012; 32: 604–612.
18. Chatelut E, Canal P, Brumner V, et al. Prediction of carboplatin clearance from standard morphological and biological patient characteristics. *J Natl Cancer Inst* 1995; 87: 573–580.
19. Bénézet S, Guimbaud R, Chatelut E, et al. How to predict carboplatin clearance from standard morphological and biological characteristics in obese patients. *Ann Oncol* 1997; 8: 607–609.
20. Smith JA. The controversy remains, a consensus is needed: how to assess renal function for dosing carboplatin. *Hematology/Oncology Pharmacy Association Newsletter*, www.hoparx.org/images/hopa/membership/newsletters/Volume-7-Issue-4-2010.pdf (2010, accessed 17 August 2018).
21. Gracia S, Montañés R, Bover J, et al. Documento de consenso: recomendaciones sobre la utilización de ecuaciones para la estimación del filtrado glomerular en adultos. *Nefrología* 2006; 26: 658–665.
22. National Kidney foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002; 39: S1–266.
23. Ainsworth NL, Marshall A, Hatcher H, et al. Evaluation of glomerular filtration rate estimation by Cockcroft-Gault, Jelliffe, Wright and Modification of Diet in Renal Disease (MDRD) formulae in oncology patients. *Ann Oncol* 2012; 23: 1845–1853.
24. Nelson WK, Formica RN Jr, Cooper DL, et al. An analysis of measured and estimated creatinine clearance rates in normal weight, overweight, and obese patients with gynecologic cancers. *J Oncol Pharm Pract* 2012; 18: 323–332.
25. Bouquegneau A, Vidal-Petiot E, Moranne O, et al. Based equations for the adjustment of drug dosage in an obese population. *Br J Clin Pharmacol* 2016; 81: 349–361.
26. Nyman HA, Dowling TC, Hudson JQ, et al. Comparative evaluation of the Cockcroft-Gault Equation and the Modification of Diet in Renal Disease (MDRD) study equation for drug dosing: an opinion of the Nephrology Practice and Research Network of the American College of Clinical Pharmacy. *Pharmacotherapy* 2011; 31: 1130–1144.
27. Shepherd ST, Gillen G, Morrison P, et al. Performance of formulae based estimates of glomerular filtration rate for carboplatin dosing in stage 1 seminoma. *Eur J Cancer* 2014; 50: 944–952.
28. Janowitz T, Williams EH, Marshall A, et al. New model for estimating glomerular filtration rate in patients with cancer. *J Clin Oncol* 2017; 35: 2798–2805.
29. Dowling TC, Wang ES, Ferrucci L, et al. Glomerular filtration rate equations overestimate creatinine clearance in older individuals enrolled in the Baltimore longitudinal study on aging: impact on renal drug dosing. *Pharmacotherapy* 2013; 33: 912–921.
30. Park EJ, Pai MP, Dong T, et al. The influence of body size descriptors on the estimation of kidney function in normal weight, overweight, obese, and morbidly obese adults. *Ann Pharmacotherapy* 2012; 46: 317–328.
31. Anglada-Martínez H, Riu-Viladoms G, do Pazo-Oubiña F, et al. Dosing of chemotherapy in obese and cachectic patients: results of a national survey. *Int J Clin Pharm* 2014; 36: 589–595.
32. Wilhelm SM and Kale-Pradhan PB. Estimating creatinine clearance: a meta-analysis. *Pharmacotherapy* 2011; 31: 658–664.