# Aligning kidney function assessment in patients with cancer to global practices in internal medicine

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## Summary

**The kidney disease: Improving Global Outcomes (KDIGO) guideline recommends assessing kidney function using glomerular filtration rate (GFR) either through direct measurement or through estimation (eGFR) and describes a standardised classification of reduced kidney function. KDIGO guidelines have been adopted by most internal medicine specialities for the assessment and classification of kidney function, but not by cancer medicine. The development of the International Consensus Guideline on Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD) aims to overcome the perceived challenges with KDIGO recommendations by describing their utility in patients with cancer. Two virtual, consensus building workshops were held consecutively, involving international, multidisciplinary participants (Part 1 of ADDIKD development). During these workshops, three consensus recommendations were agreed upon based on KDIGO's principles; to standardise kidney function assessment, classify kidney function, and determine a uniform approach to dose anticancer drugs in patients with reduced kidney function. Cancer clinicians attending the workshops identified issues regarding the adoption of KDIGO's recommendations. These issues were addressed by nephrologists, clinical pharmacologists, and other clinicians with extensive experience in the contemporary assessment of kidney function. The key concern for cancer specialists was a hesitancy to move away from the familiar and long-standing practice of using the Cockcroft–Gault equation to estimate creatinine clearance. The consensus building within the two multidisciplinary workshops allowed a thorough assessment of the evidence and clarified how directly measured GFR and eGFR, rather than creatinine clearance, could be optimally utilised in cancer care. The development of Part 1 of the ADDIKD guideline represents a standardised, contemporary approach to the assessment, classification, and utility of kidney function in the setting of cancer care and it harmonises with the approach used in other areas of medicine internationally.**

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### Research in context

#### Evidence before this study

Cancer clinicians have been slow to adopt modern kidney function assessment methods, such as estimated glomerular filtration rate (eGFR), as recommended by Kidney Disease: Improving Global Outcomes (KDIGO) guidelines. The primary barriers to implementation include a lack of familiarity with the newer techniques and a perceived effectiveness of the traditional creatinine clearance values calculated using the Cockcroft–Gault equation, particularly in the context of anticancer drug dosing.

#### Added value of this study

Over two multidisciplinary workshops, three consensus recommendations were developed as the foundation for the International Consensus Guideline on Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD). These recommendations align with KDIGO to standardise kidney function assessment and classification, establishing a uniform approach to dosing anticancer drugs in patients with reduced kidney function. The workshops addressed misconceptions regarding eGFR versus creatinine clearance and encouraged the wider use of directly measured kidney function assessments for more accurate evaluations in high-risk clinical situations.

#### Implications of all the available evidence

A standardised, contemporary approach to the assessment, classification, and utility of kidney function in cancer care harmonising with methods used in other areas of medicine internationally.

## Introduction

In clinical practice, various techniques, including estimation formulas and direct measurement of glomerular filtration rate (GFR), are employed to evaluate kidney function. The optimal method for assessing kidney function, critical for guiding clinical interventions such as drug selection and dose calculation, often presents challenges. These challenges arise from patient-specific considerations such as volume depletion, loss of muscle mass and underlying pathologies. Other considerations include the propensity to use standard dosing recommendations based on body weight or surface area, clinical resource accessibility and the narrow therapeutic index of treatments influenced by kidney function. An added complexity in cancer therapeutics is that numerous anticancer drugs cause kidney injury or are reliant on the determination of kidney function to calculate the drug dose or their suitability for inclusion

in a patient's treatment. For these reasons an accessible, reliable method of kidney function assessment is essential to the challenge of optimally dosing anticancer drugs to maximise efficacy and minimise toxicity.

The direct measurement of clearance of exogenous markers, which are freely filtered by the glomerulus without being reabsorbed or secreted by the tubules, represents the gold standard for accurate kidney function assessment, and is referred to as measured GFR. These markers include iohexol, iothalamate, $^{51}$Cr-EDTA (radioactive chromium complex with ethylene diamine tetraacetic acid) and $^{99m}$Tc-DTPA (TC-diethylene-triaminepentaacetic acid).[1] Despite its precision, this methodology is often not used due to its cost, timeliness and limited accessibility, especially when compared with other assessment methods.

In clinical settings, convenience has driven the practice of estimating kidney function based on equations using serum creatinine ($S_{Cr}$). $S_{Cr}$ is continuously released from skeletal muscle and is freely filtered by the glomerulus but is also actively secreted (20–30%) through the proximal tubule, leading to errors when used to estimate absolute GFR.[2,3] Creatinine clearance (CrCl), estimated using the Cockcroft–Gault equation, was a well-established common surrogate for GFR.[4,5] Despite being convenient and widely utilised in drug dosing, the Cockcroft–Gault equation, developed in the 1970s based on measured CrCl from 24-h urine collections, has a perceived accuracy which has not been confirmed following the use of the isotope dilution mass spectrometry standardisation of $S_{Cr}$ assay in 2010.[4–6] Furthermore, CrCl overestimates actual GFR by 10–20% as it includes creatinine filtered through the glomerulus and via tubular secretion (noting the tubular secretion of creatinine increases in certain physiological conditions i.e., advanced liver disease).[2,3] Despite these limitations, CrCl estimates remain central to the dosing of kidney eliminated anticancer drugs, for example carboplatin, methotrexate and cisplatin. Contemporary GFR estimation methods, initially the Modification of Diet in Renal Disease (MDRD),[7] and now the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) formulas,[8] incorporate updated $S_{Cr}$ assay standards and are based on direct GFR measurements using iothalamate.

The Kidney Disease: Improving Global Outcomes (KDIGO), the leading international nephrology guidelines organisation, advised in its Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease,[9,10] that clinicians should use the estimated glomerular filtration rate (eGFR) for initial kidney function assessment. Furthermore, laboratories should report eGFR using the validated CKD-EPI equations ($eGFR_{CKD\text{-}EPI}$). KDIGO defines reduced kidney function (formerly referred to as kidney impairment or dysfunction) as eGFR < 60 mL/min/1.73 $m^2$, and categorises further degrees of kidney function decline based on disease risk prediction.[10] However, these standardised nephrology guidelines are not consistently applied in oncology-haematology settings, particularly in anticancer drug dosing, where significant variations exist in evaluating and defining kidney function for dose adjustment.[11–14]

Cancer clinicians have been slow to adopt modern kidney function assessment methods, with their lack of familiarity and understanding of the newer techniques and perceived effectiveness of using the Cockcroft–Gault equation as being the primary barriers to implementing them particularly in context to anticancer drug dosing. To address this issue, we developed the International Consensus Guideline on Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD).[15] The objective of this paper is to describe how consensus was achieved for the three main recommendations from ADDIKD to provide a standardised, evidence based and practical framework for assessing and categorising kidney function in patients with cancer and thereby promoting alignment with other areas of internal medicine.

## Methods

ADDIKD was developed in two parts. Part 1 involved the formulation of three recommendations for the assessment and classification of kidney function in patients with cancer (details on the methodology of Part 1 are described by Sandhu G, Armstrong E A, Adattini J et al.[16]).

An initial virtual panel discussion comprising 26 members from the multidisciplinary ADDIKD *Content Development Working Group* and expert contributors from nephrology, pharmacometrics, clinical pharmacology, and clinical pathology was conducted. The panel aimed to establish:

1. A standardised method for assessing kidney function in patients with cancer.
2. Guidelines for applying this method to anticancer drug dosing.
3. The use of KDIGO's Chronic Kidney Disease (CKD) categories[9,10] to guide anticancer drug dosing and monitoring in patients with kidney reduced function.

Subsequently, another virtual workshop with 59 participants, including *Key External Stakeholders*, *Invited Expert Contributors*, and the *Content Working Group*, sought broader consensus on these refined recommendations.[16]

## Key recommendations and how they were achieved

Part 1 of the guideline development process provided three consensus driven recommendations through the two workshops. The workshops uncovered questions and discussion points on kidney function assessment,

largely amongst the cancer clinicians. It also provided an opportunity for expert clarification by nephrologists on these questions to aid the acceptance of the three recommendations. Below, we describe these questions raised by workshop attendees for each of the three recommendations (Panels 1–3), and the evidence and clinician experience that supported the achievement of group consensus. For full details on ADDIKD recommendations for the assessment and classification of kidney function and its broader application refer to the online version of ADDIKD [https://www.eviq.org.au/clinical-resources/addikd-guideline/4185-quick-reference-tool-anticancer-drug-dosing].[15]

### Questions raised during the workshops about recommendation 1

a) Why is CrCl not suitable for assessment of kidney function?

The consensus that emerged from both workshops was the superior accuracy of directly measured GFR when assessing kidney function in adult patients with cancer–as demonstrated by previous studies.[1,19,20] However, the practicality of directly measured GFR in clinical settings was hindered by challenges related to accessibility (especially in regional and remote settings), time and cost.[21] For these reasons, the estimation of GFR was considered a more feasible option in most contexts.

In terms of estimated GFR, $eGFR_{CKD\text{-}EPI}$ (eGFR using the 2009 CKD-EPI equation, see Supplementary Material S1) was the preferred method during the workshops because:

- It demonstrated higher accuracy and precision compared with alternative estimation approaches. Specifically, $eGFR_{CKD\text{-}EPI}$ had greater precision than CrCl calculated via the Cockcroft–Gault equation, with 84% versus 74% of values falling within a 30% range of directly measured GFR.[8] Additionally using identical variables, the CKD-EPI equation reduced bias compared with the MDRD equation when eGFR > 30 mL/min/1.73 $m^2$ (57–75% improvement),[22] and when aligning kidney function values with risk stratification categories for CKD-related outcomes.[23,24]
- It incorporates the international standardisation of the creatinine assay,[17,25,26] and hence can be used with current kidney function categories. The Cockcroft–Gault equation was developed using non-standardised creatinine assays,[4] and therefore CrCl calculations may not be as reliable when applied to current kidney function categories.[27]
- It has been tested and validated in diverse populations. This includes many thousands of patients of advanced age, with varying cancers and from multiple ethnic backgrounds.[27–31] In contrast, the Cockcroft–Gault equation was derived from a small population (n = 249) of hospitalised males who were mostly Caucasian (n = 236, 95%) with mostly normal kidney function.[4,32]
- In many countries, it is automatically reported in laboratory results when requesting $S_{Cr}$ measurement (as per recommendations from KDIGO,[33] National Kidney Foundation,[34] National Institute for Health and Care Excellence,[35] and Australasian Creatinine Consensus Working Group[17]), enabling ease of use at both the patient bedside and outpatient clinic.
- It is aligned with internationally accepted recommendations from KDIGO and enables the classification of kidney function, as per the KDIGO CKD categories and the approach applied in other areas of medicine.[9,10]

Therefore, in terms of universal accessibility and reliability in the cancer population, $eGFR_{CKD\text{-}EPI}$ was recommended as the primary alternative when directly measured GFR was not feasible.

The 2009 CKD-EPI equation predicts kidney function using the variables of age, sex, $S_{Cr}$, and, where applicable, race. Notably the 2009 version of the equation allows for an extra coefficient to account for

*Panel 1*: **Summary of recommendation 1.**

We recommend the use of estimated glomerular filtration rate calculated via the Chronic Kidney Disease—Epidemiology Collaboration ($eGFR_{CKD\text{-}EPI}$) equation to guide the assessment of kidney function, except where directly measured glomerular filtration rate (GFR) is clinically necessary.
*Evidence quality/certainty:* ***clinical consensus****; strength of recommendation:* ***strong***.

1.1 The most accurate method of assessing kidney function in adult patients with cancer is by directly measured GFR.
1.2 $eGFR_{CKD\text{-}EPI}$ is a more accurate and precise estimation of directly measured GFR than other estimation methods of kidney function. $eGFR_{CKD\text{-}EPI}$ is reported automatically in pathology results, accounts for creatinine assay standardisation, and aligns with international nephrology recommendations.
1.3 $eGFR_{CKD\text{-}EPI}$ requires stable kidney function and should be performed as close as possible to the time of administering the anticancer drug(s) to ensure it is a reflective estimation of the patient's steady state kidney function. This is especially important if the anticancer drug(s) is guided by kidney function for dosing and/or demonstrates nephrotoxic potential, where $eGFR_{CKD\text{-}EPI}$ < 60 mL/min/1.73 $m^2$, where the patient is acutely unwell (or has recently recovered from an acute illness) or displays signs of unstable kidney function (including development of acute kidney injury).
1.4 $eGFR_{CKD\text{-}EPI}$ may be unreliable in certain clinical situations involving, but not limited to, extremes of body size or muscle mass (e.g., obesity, non-obese sarcopenia, high muscle mass), amputees, persons with paraplegia or conditions of skeletal muscle, individuals with exceptional dietary habits (e.g., creatine supplements), advanced liver disease, untreated hypothyroidism, drugs interfering with creatinine secretion or the creatinine assay, and ureteric obstruction.
1.5 $eGFR_{CKD\text{-}EPI}$ is unsuitable for assessing kidney function in kidney replacement therapy, pregnant women, and patients <18 years of age.[17,18]

**Panel 2: Summary of recommendation 2.**

We recommend $eGFR_{CKD\text{-}EPI}$ to guide the dosing of anticancer drugs whose dose is dependent on kidney function, except in specific clinical situations or for a select group of anticancer drugs where $eGFR_{CKD\text{-}EPI}$ may be unsuitable.
*Evidence quality/certainty:* ***clinical consensus****; strength of recommendation:* ***strong***.

2.1 Directly measured GFR is preferred to guide the initial dosing:
- for a select group of anticancer drugs including, but not limited to, carboplatin, cisplatin, and methotrexate (≥500 mg/m$^2$).
- of anticancer drugs whose dose is dependent on kidney function in specific clinical situations involving, but not limited to, patients with extremes of body size or muscle mass, amputees, persons with paraplegia or conditions of skeletal muscle.

2.2 $eGFR_{CKD\text{-}EPI}$ adjusted to an individual's body surface area (BSA) is not routinely advised to guide dosing of anticancer drugs over standardised $eGFR_{CKD\text{-}EPI}$, except for carboplatin. Anticancer drug dosing based on weight descriptors (e.g., BSA, weight) may impact the performance of BSA-adjusted $eGFR_{CKD\text{-}EPI}$ to guide dosing, especially, as body size/composition will be accounted for twice in dose calculation.

2.3 BSA-adjusted $eGFR_{CKD\text{-}EPI}$ is a suitable alternative to directly measured GFR for use in the Calvert formula when dosing carboplatin, especially where $eGFR_{CKD\text{-}EPI}$ 45–125 mL/min/1.73 m$^2$, treatment intent is non-curative and the patient is neither an amputee, paraplegic or has conditions of skeletal muscle and is without extremes of body size or muscle mass. Directly measured GFR is the preferred kidney function value in other clinical situations.

2.4 When dosing anticancer drugs in the presence of reduced kidney function, carefully consider:
- Patient factors—clinical condition (e.g., hydration status, performance status), comorbidities (e.g., liver dysfunction), genetic polymorphisms (if applicable), factors influencing kidney function (e.g., presence of a single or horseshoe kidney, kidney transplant, dialysis) and attitude/beliefs towards treatment.
- Treatment factors—treatment protocol (e.g., intent of treatment, appropriate alternative treatment protocols with similar efficacy and without drugs dependent on kidney function for dosing), risk of adverse events (e.g., tumour lysis syndrome), anticancer drug properties (e.g., pharmacokinetics, pharmacodynamics, formulation, availability of therapeutic drug monitoring), and concomitant drugs (especially with nephrotoxic potential).
- Other—accessibility to directly measured GFR, and the evidence and strength behind dose recommendations

individuals of African American ancestry having higher $S_{Cr}$ compared to individuals of non-African American ancestry.[8] Outside of North America, the 2009 CKD-EPI equation has been largely implemented in clinical practice without the race coefficient.[17,35] In 2021, the National Kidney Foundation and American Society of Nephrology Task Force recommended refitting the 2009 CKD-EPI equation without race, citing that race was a social rather than a biological construct.[36] eGFR calculated with the refitted equation delivered more precision to directly measured GFR with individuals who previously used the race coefficient, but overestimated eGFR by ~3.9 mL/min/1.73 m$^2$ in other populations.[37] Although KDIGO has recently endorsed the 2021 CKD-EPI equation,[10] at the time of ADDIKD's publication the working group consensus was to continue with the 2009 CKD-EPI equation (without the race component) throughout the guideline. However, in countries that have since adopted the 2021 CKD-EPI equation, it may be acceptable to replace references of the 2009 CKD-EPI equation in any recommendations with the 2021 equation.

b) Are there conditions where $eGFR_{CKD\text{-}EPI}$ should not be used?

During the workshops, nephrologists, pharmacologists, and cancer clinicians unanimously agreed on clinical situations where kidney function estimations may not be unsuitable or less reliable. As per the literature, $eGFR_{CKD\text{-}EPI}$ was deemed unsuitable for assessing kidney function in patients with cancer who were either pregnant, <18 years old, with acute kidney injury (AKI) or undergoing kidney replacement therapy (KRT) and was therefore outside the scope of the guideline.[10,38]

The contribution of non-GFR determinants of $S_{Cr}$ e.g., diet, muscle mass are the likely sources of error in assessing $eGFR_{CKD\text{-}EPI}$ (hence reducing its reliability).[10] Some examples and alternative methods to assess

**Panel 3: Summary of recommendation 3.**

We recommend the Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease (CKD)[9,10] categories to guide the stepwise dose adjustment of anticancer drugs in reduced kidney function and the monitoring of drug-related adverse events.
*Evidence quality/certainty:* ***clinical consensus****; strength of recommendation:* ***strong***.

kidney function for these situations was robustly discussed by the participants in both workshops resulting in several pragmatic consensus approaches (Table 1). The full list of clinical situations where $eGFR_{CKD\text{-}EPI}$ may be unreliable is provided in the ADDIKD guideline.[15]

$eGFR_{CKD\text{-}EPI}$ is indexed to a standardised body surface area (BSA) of 1.73 $m^2$ to enable comparison of kidney function between individuals with different body sizes with the assumption that BSA is a reliable indicator of kidney size and expressed in mL/min/1.73 $m^2$, compared to CrCl estimated using Cockcroft–Gault which is not normalised to BSA (expressed as mL/min).[8,51] The applicability of the BSA reference value of 1.73 $m^2$ to the larger-sized contemporary population has been questioned,[52,53] and at extremes of body size the discordance between kidney $eGFR_{CKD\text{-}EPI}$ and actual GFR appears to be more significant (Table 1). $eGFR_{CKD\text{-}EPI}$ adjusted for BSA (expressed as mL/min), incorporates body size parameters into the $eGFR_{CKD\text{-}EPI}$ value by removing the 1.73 $m^2$ standardisation (where individual BSAs are much larger than the 1.73 $m^2$ indexing). Several studies have demonstrated BSA-adjusted $eGFR_{CKD\text{-}EPI}$ values are closer to directly measured GFR (in mL/min) than BSA-standardised $eGFR_{CKD\text{-}EPI}$.[31,40,41] However, there are conflicting reports regarding the performance of BSA-adjusted $eGFR_{CKD\text{-}EPI}$ in comparison to CrCl using alternative weight descriptors in this cohort, particularly with BMI > 40 kg/$m^2$.[42,43]

Following the publication of ADDIDK, KDIGO recently updated its guidance to consider incorporating serum cystatin C ($S_{Cys}$) [another endogenous filtration marker] or a combination of both $S_{Cr}$ and $S_{Cys}$ in the CKD-EPI equation to improve the accuracy of eGFR impacted by error from non-GFR determinants of $S_{Cr}$ e.g., non-obese sarcopenia, exceptional dietary intake.[10]

c) Is it acceptable to use prior $eGFR_{CKD\text{-}EPI}$ values rather than obtaining a value on the day of treatment?

Due to the practicality of repeating blood tests in some settings, a portion of cancer clinicians in the workshop questioned the acceptability of using kidney function values either several days or a week prior to starting anticancer drug treatment. The clinical consensus amongst workshop participants was that kidney function assessment occurs at the beginning of anticancer drug treatment (first cycle) and should be considered prior to subsequent cycles of anticancer drug treatment, especially if:

- the dose of the anticancer drug should be adjusted in the presence of reduced kidney function. Approximately 80% of patients undergoing anticancer drug

| Clinical situation | Recommendations to assess kidney function |
|---|---|
| Obesity (BMI ≥ 30 kg/$m^2$) | • Directly mGFR is the most accurate and strongly preferred.[39]<br>• Estimation methods may be considered for their practicality within the clinical situation, [e.g., BSA-adjusted $eGFR_{CKD\text{-}EPI}$,[31,40,41] CrCl using alternative weight descriptors[42,43]] noting their overall inferiority in this cohort. |
| Non-obese sarcopenia | • Directly mGFR is the most accurate and strongly preferred.[1,10]<br>• eGFR using the CKD-EPI equation with $S_{Cys}$ instead of $S_{Cr}$.[44] Issues with accessing $S_{Cys}$, and that cancer cells may incidentally produce cystatin C (leading to underestimation of eGFR).[45] |
| Conditions of skeletal muscle, paraplegia, or amputees | • Directly mGFR is the most accurate and strongly preferred.[1,10]<br>• 24-h urine collection for measuring CrCl may be useful if directly mGFR is not accessible, noting the limitations with collecting an accurate sample.[39,46] |
| Exceptional dietary intake (e.g., vegetarian diet, high protein diet, creatine supplements) | • Directly mGFR is the most accurate and strongly preferred.[1,10]<br>• 24-h urine collection for measuring CrCl may be useful if directly mGFR is not accessible, noting the limitations with collecting an accurate sample. |
| Advanced liver disease | • Directly mGFR is the most accurate and strongly preferred or eGFR using the CKD-EPI equation with $S_{Cys}$ instead of $S_{Cr}$.[47,48]<br>• 24-h urine collection for measuring CrCl may be appropriate if other methods are not accessible, noting the limitations with collecting an accurate sample.[49] |
| Transgender population | • Directly mGFR is the most accurate.[50]<br>• Calculation of $eGFR_{CKD\text{-}EPI}$ using both male and female coefficients to indicate the range of kidney function in transgender persons on gender-affirming hormone therapy.[50] |
| Bone marrow transplant patients | • Not specifically included within the scope of ADDIKD although the application of the guideline recommendations for the assessment of kidney function in a bone marrow transplant setting may be suitable based on clinical judgement. |

BMI—body mass index; BSA—body surface area; CKD-EPI—Chronic Kidney Disease-Epidemiology Collaboration; CrCl—creatinine clearance; GFR—glomerular filtration rate; eGFR—estimated glomerular filtration rate; $eGFR_{CKD\text{-}EPI}$—estimated glomerular filtration rate using Chronic Kidney Disease-Epidemiology formula; mGFR—measured glomerular filtration rate; $S_{Cr}$—serum creatinine; $S_{Cys}$—serum cystatin C.

***Table 1:*** **Recommendations to assess kidney function in clinical situations where $eGFR_{CKD\text{-}EPI}$ may be unreliable.[15]**

treatment receive at least one anticancer drug that requires dose adjustment for reduced kidney function.[54,55]
- the anticancer drug has the potential to cause nephrotoxicity. Over 80% of patients with cancer receive at least one anticancer drug with significant nephrotoxic potential.[56,57]
- the patient has experienced acute illness in the previous cycle of treatment or during the current cycle.
- the patient does not have stable kidney function. Examples of clinical situations in which this occurs include urinary obstruction, kidney involvement because of the malignancy [e.g., multiple myeloma], fluctuating volume status or AKI. Up to 59% of patients with cancer will develop AKI with 7–12% progressing to KRT).[58–60] Contributing factors include drug-related AKI (up to 9% directly from anticancer drug treatment), sepsis, hypovolaemia, tumour lysis syndrome and urinary tract obstruction.[58–60]

Participants of both workshops agreed that a reminder within ADDIKD was required for clinicians to cautiously interpret $S_{Cr}$-based estimates (such as $eGFR_{CKD\text{-}EPI}$) in the acutely ill or patients who demonstrate rapidly changing kidney function, noting that peaks in $S_{Cr}$ can lag 24–72 h after kidney injury.[61]

### Questions during the workshops about recommendation 2

a) Will it be confusing for clinicians if existing guidance on dosing chemotherapy in reduced kidney function contradicts recommendation 2?

The conflicting information in established guidance for anticancer drug dosing in reduced kidney function was a considerable concern for cancer clinicians. Part of this concern related to prescribing in a manner that was not consistent with the product information, historical practice, or the lack of validation for use of $eGFR_{CKD\text{-}EPI}$ in this setting (specific examples in Sandhu G, Adattini J, Armstrong E A et al.,[62]).

The European Medicines Agency (EMA)[39] and the United States Food and Drug Administration (FDA)[44] guidelines on drug development submissions in reduced kidney function recommend GFR for the assessment of kidney function, with EMA specifically recommending directly measured GFR, whilst the FDA endorsing BSA-adjusted eGFR alongside CrCl as options. However, early drug development studies investigating kidney drug clearance require further consideration, as eGFR (including BSA-adjusted eGFR) and CrCl, unlike directly measured GFR, may not adequately capture changes to clearance by the kidneys with drugs that undergo extensive tubular secretion.[45,56]

Although CrCl calculated via the Cockcroft–Gault equation has been used historically to guide dosing in reduced kidney function, it lacks applicability to current anticancer drug dosing as older studies estimated CrCl using non-standardised creatinine assays.[27] Costa et al., observed that in 1200 patients with solid tumours, $eGFR_{CKD\text{-}EPI}$ predicted directly measured GFR more accurately than CrCl calculated via Cockcroft–Gault equation.[29] Certainly, in carboplatin and cisplatin, $eGFR_{CKD\text{-}EPI}$ demonstrates more precision than CrCl in assessing kidney function for drug dosing.[46] Comparisons of eGFR versus CrCl predictions in patients receiving non-cancer drugs have suggested that 88% of patients with reduced kidney function did not have a change in dose regardless of the estimation method.[47] Part 2 of ADDIKD's development addresses the drug dosing issue through individual drug workshops where pharmacokinetic and pharmacodynamic evidence along with ADDIKD's three key recommendations discussions were evaluated to determine the dosing approach for specific anticancer drugs.[16,62]

Recently KDIGO has supported ADDIKD's recommendations in the use of $eGFR_{CKD\text{-}EPI}$ to guide anticancer drug dose adjustment except where directly measured GFR was recommended. These include clinical situations where $eGFR_{CKD\text{-}EPI}$ may be unreliable or in a select group of anticancer drugs, such as with the administration of cisplatin, methotrexate or carboplatin]).[10]

Collectively, a pragmatic approach to dosing in reduced kidney function was deemed essential during the workshops. Consideration of the clinical risk-benefit of administering a particular dose was stressed throughout ADDIKD,[15] highlighting the patient's clinical status, comorbidities, treatment protocol, beliefs/attitudes towards treatment, anticancer drug properties, concomitant medicines, accessibility to directly measured GFR, availability of therapeutic drug monitoring and the evidence and strength behind dose recommendations (Supplementary Material S2).

b) Should $eGFR_{CKD\text{-}EPI}$ adjusted to body surface area be used for all drug dosing in reduced kidney function?

As previously mentioned, the applicability of the BSA reference value of 1.73 $m^2$ for $eGFR_{CKD\text{-}EPI}$ indexation may not suitable with varying body sizes.[52,53] Although FDA promotes the use of BSA-adjusted $eGFR_{CKD\text{-}EPI}$, this may not be relevant to all anticancer drugs.

Anticancer drug dosing based on weight descriptors (e.g., BSA, weight) may impact the performance of BSA-adjusted $eGFR_{CKD\text{-}EPI}$ (expressed as mL/min) to guide dosing, as body size/composition will be accounted for twice to individualise doses.[48,49,52,53] When dosing capecitabine in $mg/m^2$ and utilising BSA-adjusted $eGFR_{CKD\text{-}EPI}$ to determine dose adjustments in reduced kidney function, patients with a lower BSA were underdosed and conversely those with a larger BSA were overdosed, despite both groups having the same standardised

$eGFR_{CKD\text{-}EPI}$.[50] When aminoglycosides were dosed in mg/kg, it was found that BSA-adjusted $eGFR_{CKD\text{-}EPI}$ guided dosing was less precise than standardised $eGFR_{CKD\text{-}EPI}$ in predicting drug clearance in overweight and obese patients.[63] The clearance of ganciclovir (dosed in mg/kg) correlated similarly with standardised and BSA-adjusted $eGFR_{CKD\text{-}EPI}$ in patients without extremes of body size.[64]

Based on this reasoning, the clinical consensus was not to routinely use BSA-adjusted $eGFR_{CKD\text{-}EPI}$ to guide dosing over standardised $eGFR_{CKD\text{-}EPI}$ (except for carboplatin).[15]

c) Why are we changing from using CrCl to calculate carboplatin doses now when historically that is how it's always been calculated in the Calvert formula?

Carboplatin is primarily eliminated through the kidneys, and Calvert et al. demonstrated the area under the curve (AUC) rather than mg/$m^2$ method for dose calculation was more useful in predicting the risk of carboplatin-related toxicity (e.g., myelosuppression) in reduced kidney function.[65] The development of the Calvert formula used directly measured GFR to calculate carboplatin doses. However, for decades, oncologists have used CrCl in the Calvert formula to calculate carboplatin doses, especially since the ground-breaking study that determined the target AUC used CrCl.[66]

Following discussion and review of data on accuracy of the various kidney function estimates and their application in the Calvert formula, the clinical consensus was that directly measured GFR is the preferred kidney function value when calculating carboplatin doses with the Calvert formula for any kidney function. BSA-adjusted $eGFR_{CKD\text{-}EPI}$ is a suitable alternative to directly measured GFR for use in the Calvert formula when dosing carboplatin, especially where $eGFR_{CKD\text{-}EPI}$ 45–125 mL/min/1.73 $m^2$ (reliability of estimated kidney function reduces outside this range),[67] treatment intent is non-curative and the patient is neither an amputee, paraplegic nor has conditions of skeletal muscle and is without extremes of body size or muscle mass.[15] BSA-adjusted $eGFR_{CKD\text{-}EPI}$ in the Calvert formula demonstrates more precision towards directly measured GFR than standardised $eGFR_{CKD\text{-}EPI}$,[31,41] and is a suitable alternative when directly measured GFR is unavailable in specific circumstances.

As an example, a demonstration of the variance between different kidney function estimations and their subsequent carboplatin doses for a hypothetical 65-year-old male patient weighing 67 kg with a height of 170 cm, a $S_{cr}$ of 97 µmol/L and a target AUC of 5 is shown in Table 2. CrCl and BSA-adjusted $eGFR_{CKD\text{-}EPI}$ varied by 8.4 mL/min resulting in a 9% difference in calculated carboplatin doses. Whether this 9% dose difference would result in a significant change in carboplatin exposure and clinical outcomes is unknown, it highlighted the importance of directly measured GFR and also the potential of CrCl in over- or under-dosing (if BSA-adjusted $eGFR_{CKD\text{-}EPI}$ has more precision to directly measured GFR).

| Kidney function assessment | Estimated kidney function | Carboplatin dose (mg)[a] |
|---|---|---|
| Creatinine clearance via Cockcroft–Gault formula | 63.6 mL/min | 443 |
| eGFR via CKD-EPI equation | 70 mL/min/1.73 $m^2$ | 475 |
| BSA-adjusted eGFR via CKD-EPI equation | 72 mL/min | 485 |

BSA—body surface area [calculated using Mosteller formula]; CKD-EPI—Chronic Kidney Disease-Epidemiology Collaboration; eGFR—estimated glomerular filtration rate; eGFR—estimated glomerular filtration rate; CKD-EPI—Chronic Kidney Disease-Epidemiology formula. [a]Calculated via Calvert formula using target area under the curve = 5.

*Table 2*: **Comparison of kidney function estimations and carboplatin doses via the Calvert formula for a 65-year-old male patient (weight = 67 kg, height = 170 cm, serum creatinine = 97 µmol/L).**

### Questions during the workshops about recommendation 3

a) Will extrapolating data from older studies correlate appropriately with the new GFR classifications?

Approximately 15–20% of patients with cancer have an eGFR 30–59 mL/min/1.73 $m^2$,[54,55] a kidney function range where many anticancer drugs have pre-defined dose adjustments or exclusions.[68,69] The most accurate kidney function assessment is of particular importance in this cohort as small variations in kidney function may place patients in CKD categories that preclude them from receiving drug therapy or at thresholds for significant dose adjustments.

There are limited studies assessing the application of KDIGO CKD categories (Supplementary Material S3),[9,10,70,71] in the dose adjustment of anticancer drugs and the monitoring of drug-related adverse events. However, during the workshops, there was unanimous agreement that standardisation of kidney function classification across clinical settings reduces the complexity of kidney function estimation and promotes uniformity to guide decision making.

## Outstanding questions

The development of the three consensus recommendations were the foundational blocks underpinning the ADDIKD guideline[15] and enabled the development of dosing recommendations in reduced kidney function for specific anticancer drugs. The workshops revealed the way in which assessment of kidney function in the setting of cancer treatment had deviated over time from contemporary approaches used in nephrology and other areas of medicine. Cancer clinicians were concerned about the risk of adopting $eGFR_{CKD\text{-}EPI}$ and noted that while directly measured GFR was acceptable, it was often not readily available. The consensus building within the two workshops promoted engagement

between multidisciplinary experts to thoroughly assess the emerging evidence and discuss practicalities of $eGFR_{CKD\text{-}EPI}$ and directly measured GFR. Most importantly, it enabled peer-to-peer learning and demystified some of the unknowns surrounding proposed changes to kidney function assessment. Although during the final workshop, participants were unanimous in support of the three recommendations, it was clear that the greatest barriers to adopting ADDIKD's recommendations were the multidisciplinary cancer clinician unawareness of the limitations when CrCl was calculated via the Cockcroft–Gault equation, the improved guidance newer kidney function assessments provided especially in the setting of reduced kidney function and the concerns regarding the evidence of these newer kidney function assessments to guide anticancer drug dosing. Further, the adoption of the ADDIKD guideline would facilitate benchmarking kidney function assessment and classification within cancer care internationally and provides a tool for instigating clinician behaviour change in this specific area of cancer medicine.

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Writing—reviewing/editing–all authors.
All authors provided critical revision of the manuscript for important intellectual content and gave approval of the submission of the manuscript for publication. GS, RLW and JA accessed and verified data in the study for publication, and GS and RLW had final responsibility for the decision to submit for publication.

#### Data sharing statement

None.

#### Declaration of interests

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**References**

1 Malyszko J, Lee MW, Capasso G, et al. How to assess kidney function in oncology patients. *Kidney Int*. 2020;97(5):894–903.
2 Kooman JP. Estimation of renal function in patients with chronic kidney disease. *J Magn Reson Imaging*. 2009;30(6):1341–1346.
3 Proulx NL, Akbari A, Garg AX, Rostom A, Jaffey J, Clark HD. Measured creatinine clearance from timed urine collections substantially overestimates glomerular filtration rate in patients with liver cirrhosis: a systematic review and individual patient meta-analysis. *Nephrol Dial Transplant*. 2005;20(8):1617–1622.
4 Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron*. 1976;16(1):31–41.
5 Hudson JQ, Nolin TD. Pragmatic use of kidney function estimates for drug dosing: the tide is turning. *Adv Chronic Kidney Dis*. 2018;25(1):14–20.
6 Piéroni L, Delanaye P, Boutten A, et al. A multicentric evaluation of IDMS-traceable creatinine enzymatic assays. *Clin Chim Acta*. 2011;412(23):2070–2075.
7 Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med*. 1999;130(6):461–470.
8 Levey A, Stevens L, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150(9):604–612.
9 Kidney Disease Improving Global Outcomes. KDIGO 2012 Clinical Practice Guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2013;3(1).
10 Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. Clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int*. 2024;105:S117–S314.
11 Australian medicines handbook. *Prescribing in renal impairment*; 2022, 2022. https://amhonline.amh.net.au. Accessed April 1, 2022.
12 BC Cancer. *Cancer drug manual*; 2022. http://www.bccancer.bc.ca/health-professionals/clinical-resources/cancer-drug-manual. Accessed April 1, 2022.
13 Hendrayana T, Wilmer A, Kurth V, Schmidt-Wolf IG, Jaehde U. Anticancer dose adjustment for patients with renal and hepatic dysfunction: from scientific evidence to clinical application. *Sci Pharm*. 2017;85(1).
14 University College London Hospitals NHS Foundation Trust. *Dose adjustment for cytotoxics in renal impairment*; 2009. http://www.londoncancer.org/media/65600/renal-impairment-dosage-adjustment-for-cytotoxics.pdf. Accessed April 1, 2022.
15 Sandhu G, Adattini J, Gordon EA, O'Neill N, On behalf of the ADDIKD Guideline Working Group. *International consensus guideline on anticancer drug dosing in kidney dysfunction*; 2022. https://www.eviq.org.au/clinical-resources/addikd-guideline/4174-anticancer-drug-dosing-in-kidney-dysfunction. Accessed July 31, 2024.
16 Sandhu G, Gordon EA, Adattini J, et al. A methodology for determining dosing recommendations for anticancer drugs in patients with reduced kidney function. *eClinicalMedicine*. 2025;82:103101. https://doi.org/10.1016/j.eclinm.2025.103101.
17 Johnson DW, Jones GRD, Mathew TH, et al. Chronic kidney disease and automatic reporting of estimated glomerular filtration rate: new developments and revised recommendations. *Med J Aust*. 2012;197(4):222–223.
18 Mathew TH, The Australasian Creatinine Consensus Working Group. Chronic kidney disease and automatic reporting of estimated glomerular filtration rate: a position statement. *Med J Aust*. 2005;183(3):138–141.
19 Cathomas R, Klingbiel D, Geldart TR, et al. Relevant risk of carboplatin underdosing in cancer patients with normal renal function using estimated GFR: lessons from a stage I seminoma cohort. *Ann Oncol*. 2014;25(8):1591–1597.
20 Oliver RTD, Mead GM, Rustin GJ, et al. Randomized trial of carboplatin versus radiotherapy for stage I seminoma: mature results on relapse and contralateral testis cancer rates in MRC TE19/EORTC 30982 study (ISRCTN27163214). *J Clin Oncol*. 2011;29(8):957–962.
21 Sprangers B, Abudayyeh A, Latcha S, Perazella MA, Jhaveri KD. How to determine kidney function in cancer patients? *Eur J Cancer*. 2020;132:141–149.
22 Stevens LA, Schmid CH, Greene T, et al. Comparative performance of the CKD Epidemiology collaboration (CKD-EPI) and the modification of diet in renal disease (MDRD) study equations for estimating GFR levels above 60 mL/min/1.73 m2. *Am J Kidney Dis*. 2010;56(3):486–495.
23 Matsushita K, Selvin E, Bash LD, Astor BC, Coresh J. Risk implications of the new CKD Epidemiology collaboration (CKD-EPI) equation compared with the MDRD study equation for estimated GFR: the atherosclerosis risk in communities (ARIC) study. *Am J Kidney Dis*. 2010;55(4):648–659.
24 White SL, Polkinghorne KR, Atkins RC, Chadban SJ. Comparison of the prevalence and mortality risk of CKD in Australia using the CKD Epidemiology collaboration (CKD-EPI) and modification of diet in renal disease (MDRD) study GFR estimating equations: the AusDiab (Australian diabetes, obesity and lifestyle) study. *Am J Kidney Dis*. 2010;55(4):660–670.
25 Johnson D, Jones G, Mathew T, et al. Chronic kidney disease and automatic reporting of estimated glomerular filtration rate: revised recommendations. *Med J Aust*. 2007;187:459–463.
26 Levey AS, Stevens LA. Estimating GFR using the CKD Epidemiology Collaboration (CKD-EPI) Creatinine Equation: more accurate GFR estimates, lower CKD prevalence estimates, and better risk predictions. *Am J Kidney Dis*. 2010;55(4):622–627.
27 Rhee J, Kwon JM, Han SH, et al. Cockcroft-Gault, Modification of Diet in Renal Disease, and Chronic Kidney Disease Epidemiology Collaboration equations for estimating glomerular filtration rates in cancer patients receiving cisplatin-based chemotherapy. *Kidney Res Clin Pract*. 2017;36(4):342–348.
28 Maple-Brown LJ, Ekinci EI, Hughes JT, et al. Performance of formulas for estimating glomerular filtration rate in Indigenous Australians with and without type 2 diabetes: the eGFR study. *Diabet Med*. 2014;31(7):829–838.
29 Costa ESVT, Gil LA Jr, Inker LA, et al. A prospective cross-sectional study estimated glomerular filtration rate from creatinine and cystatin C in adults with solid tumors. *Kidney Int*. 2022;101:1523–1755 (Electronic).
30 Stevens LA, Claybon MA, Schmid CH, et al. Evaluation of the Chronic Kidney Disease Epidemiology Collaboration equation for estimating the glomerular filtration rate in multiple ethnicities. *Kidney Int*. 2011;79(5):555–562.
31 Janowitz T, Williams EH, Marshall A, et al. New model for estimating glomerular filtration rate in patients with cancer. *J Clin Oncol*. 2017;35(24):2798–2805.
32 Scappaticci GB, Regal RE. Cockcroft-Gault revisited: new de-liverance on recommendations for use in cirrhosis. *World J Hepatol*. 2017;9(3):131–138.
33 Kidney Disease Improving Global Outcomes (KDIGO). *KDIGO Clinical Practice Guideline for acute kidney injury*; 2012. kdigo.org/wpcontent/uploads/2016/10/KDIGO-2012-AKI-Guideline-English.pdf. Accessed March 31, 2022.
34 Inker LA, Astor BC, Fox CH, et al. KDOQI US commentary on the 2012 KDIGO Clinical Practice Guideline for the evaluation and management of CKD. *Am J Kidney Dis*. 2014;63(5):713–735.
35 National Institute for Health and Care Excellence. *Chronic kidney disease: assessment and management*; 2021. https://www.nice.org.uk/guidance/ng203. Accessed March 31, 2022.
36 Delgado C, Baweja M, Crews DC, et al. A unifying approach for GFR estimation: recommendations of the NKF-ASN Task Force on reassessing the inclusion of race in diagnosing kidney disease. *J Am Soc Nephrol*. 2021;32(12):2994.
37 Inker LA, Eneanya ND, Coresh J, et al. New creatinine- and cystatin C–based equations to estimate GFR without race. *N Engl J Med*. 2021;385(19):1737–1749.
38 Mirkov S, Scuderi C, Lloyd J, et al. Estimation of kidney function for medication dosing in adult patients with chronic kidney disease: a practice update. *J Pharm Pract Res*. 2024;54(1):94–106.
39 European Medicines Agency. *Guideline on the evaluation of the pharmacokinetics of medicinal products in patients with decreased renal function*; 2015. https://doi.org/10.1016/j.eclinm.2025.103161. https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-evaluation-pharmacokinetics-medicinal-products-patients-decreased-renal-function_en.pdf. Accessed March 25, 2022.
40 Chancharoenthana W, Wattanatorn S, Vadcharavivad S, Eiam-Ong S, Leelahavanichkul A. Agreement and precision analyses of various estimated glomerular filtration rate formulae in cancer patients. *Sci Rep*. 2019;9(1):19356.

41 Chew-Harris JS, Chin PK, Florkowski CM, George P, Endre Z. Removal of body surface area normalisation improves raw-measured glomerular filtration rate estimation by the Chronic Kidney Disease Epidemiology Collaboration equation and drug dosing in the obese. *Intern Med J*. 2015;45(7):766–773.
42 López-Martínez M, Luis-Lima S, Morales E, et al. The estimation of GFR and the adjustment for BSA in overweight and obesity: a dreadful combination of two errors. *Int J Obes*. 2020;44(5):1129–1140.
43 Pai M. Estimating the glomerular filtration rate in obese adult patients for drug dosing. *Adv Chronic Kidney Dis*. 2010;17(5):e53–e62.
44 Food and Drug Administration–Center for Drug Evaluation and Research. *Pharmacokinetics in patients with impaired renal function - study design, data analysis, and impact on dosing*; 2020. https://www.fda.gov/media/78573/download. Accessed March 25, 2022.
45 Chapron A, Shen DD, Kestenbaum BR, Robinson-Cohen C, Himmelfarb J, Yeung CK. Does secretory clearance follow glomerular filtration rate in chronic kidney diseases? Reconsidering the intact nephron hypothesis. *Clin Transl Sci*. 2017;10(5):395–403.
46 Funakoshi Y, Fujiwara Y, Kiyota N, et al. Validity of new methods to evaluate renal function in cancer patients treated with cisplatin. *Cancer Chemother Pharmacol*. 2016;77(2):281–288.
47 Park EJ, Wu K, Mi Z, et al. A systematic comparison of cockcroft-gault and modification of diet in renal disease equations for classification of kidney dysfunction and dosage adjustment. *Ann Pharmacother*. 2012;46(9):1174–1187.
48 Horie S, Oya M, Nangaku M, et al. Guidelines for treatment of renal injury during cancer chemotherapy 2016. *Clin Exp Nephrol*. 2018;22(1):210–244.
49 Murray PT, Ratain MJ. Estimation of the glomerular filtration rate in cancer patients: a new formula for new drugs. *J Clin Oncol*. 2003;21(14):2633–2635.
50 Ratain MJ. Dear doctor: we really are not sure what dose of capecitabine you should prescribe for your patient. *J Clin Oncol*. 2002;20(6):1434–1435.
51 Möller E, McIntosh JF, Van Slyke DD. Studies of urea excretion II: relationship between urine volume and the rate of urea excretion by normal adults. *J Clin Investig*. 1928;6(3):427–465.
52 Sprangers B, Sandhu G, Rosner MH, Tesarová P, Stadler WM, Malyszko J. Drug dosing in cancer patients with decreased kidney function: a practical approach. *Cancer Treat Rev*. 2020;93:102139.
53 Casal MA, Nolin TD, Beumer JH. Estimation of kidney function in oncology: implications for anticancer drug selection and dosing. *Clin J Am Soc Nephrol*. 2019;14(4):587–595.
54 Janus N, Launay-vacher V, Byloos E, et al. Cancer and renal insufficiency results of the BIRMA study. *Br J Cancer*. 2010;103(12):1815–1821.
55 Launay-Vacher V, Oudard S, Janus N, et al. Prevalence of renal insufficiency in cancer patients and implications for anticancer drug management: the renal insufficiency and anticancer medications (IRMA) study. *Cancer*. 2007;110(6):1376–1384.
56 Pradhan S, Wright DFB, Duffull SB. Evaluation of designs for renal drug studies based on the European Medicines Agency and Food and Drug Administration guidelines for drugs that are predominantly secreted. *Br J Clin Pharmacol*. 2021;87(3):1401–1410.
57 Winter MA, Guhr KN, Berg GM. Impact of various body weights and serum creatinine concentrations on the bias and accuracy of the Cockcroft-Gault equation. *Pharmacotherapy*. 2012;32(7):604–612.
58 Christiansen CF, Johansen MB, Langeberg WJ, Fryzek JP, Sørensen HT. Incidence of acute kidney injury in cancer patients: a Danish population-based cohort study. *Eur J Intern Med*. 2011;22(4):399–406.
59 Kitchlu A, McArthur E, Amir E, et al. Acute kidney injury in patients receiving systemic treatment for cancer: a population-based cohort study. *J Natl Cancer Inst*. 2019;111(7):727–736.
60 Kemlin D, Biard L, Kerhuel L, et al. Acute kidney injury in critically ill patients with solid tumours. *Nephrol Dial Transplant*. 2018;33(11):1997–2005.
61 Launay-Vacher V, Izzedine H, Rey JB, et al. Incidence of renal insufficiency in cancer patients and evaluation of information available on the use of anticancer drugs in renally impaired patients. *Med Sci Monit*. 2004;10(5):Cr209–Cr212.
62 Sandhu G, Adattini J, Armstrong AE, et al. *Prescribers guide to the application of international consensus guideline for anticancer drug dosing in kidney dysfunction in cancer treatment [unpublished]*. 2024.
63 Pai MP, Nafziger AN, Bertino JS Jr. Simplified estimation of aminoglycoside pharmacokinetics in underweight and obese adult patients. *Antimicrob Agents Chemother*. 2011;55(9):4006–4011.
64 Palacio-Lacambra M-E, Comas-Reixach I, Blanco-Grau A, Suñé-Negre J-M, Segarra-Medrano A, Montoro-Ronsano J-B. Comparison of the Cockcroft-Gault, MDRD and CKD-EPI equations for estimating ganciclovir clearance. *Br J Clin Pharmacol*. 2018;84(9):2120–2128.
65 Calvert AH, Newell DR, Gumbrell LA, et al. Carboplatin dosage: prospective evaluation of a simple formula based on renal function. *J Clin Oncol*. 1989;7(11):1748–1756.
66 Jodrell DI, Egorin MJ, Canetta RM, et al. Relationships between carboplatin exposure and tumor response and toxicity in patients with ovarian cancer. *J Clin Oncol*. 1992;10(4):520–528.
67 Oguri T, Shimokata T, Ito I, et al. Extension of the Calvert formula to patients with severe renal insufficiency. *Cancer Chemother Pharmacol*. 2015;76(1):53–59.
68 Kintzel PE, Dorr RT. Anticancer drug renal toxicity and elimination: dosing guidelines for altered renal function. *Cancer Treat Rev*. 1995;21(1):33–64.
69 Lichtman SM, Wildiers H, Launay-Vacher V, Steer C, Chatelut E, Aapro M. International Society of Geriatric Oncology (SIOG) recommendations for the adjustment of dosing in elderly cancer patients with renal insufficiency. *Eur J Cancer*. 2007;43(1):14–34.
70 Beumer JH, Inker LA, Levey AS. Improving carboplatin dosing based on estimated GFR. *Am J Kidney Dis*. 2018;71(2):163–165.
71 Levey AS, Eckardt K-U, Dorman NM, et al. Nomenclature for kidney function and disease: report of a kidney disease: improving global outcomes (KDIGO) consensus conference. *Kidney Int*. 2020;97(6):1117–1129.