Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction:
National consensus on a standardised approach to measuring kidney function in cancer patients and its application to anticancer drug dosing

Background

Anticancer drug dosing recommendations in kidney dysfunction are often empirical, based on non-standardised creatinine assays calculated via the Cockcroft-Gault equation,[1] and lack applicability to globally accepted kidney dysfunction classifications.

The guideline aims to provide a consensus-based standardised approach to the assessment of kidney function in cancer patients and its application to anticancer drug dosing.

Method

An international multidisciplinary guideline working group was established to develop the *International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction* (ADDIKD), using the best practice guideline development framework.[2] The working party comprised expert medical oncologists, haematologists, nephrologists, pharmacists, clinical pharmacologists and guideline development specialists with representation from key groups including International Society of Geriatric Oncology, Cancer and the Kidney International Network, National Cancer Institute's Organ Dysfunction Working Group and Kidney Disease Improving Global Outcomes (KDIGO). The working group drafted three main recommendations that underpin the consistency and progress of ADDIKD.

A virtual workshop was held in December 2020 inviting national external stakeholders in cancer care, nephrology, clinical pharmacology, academia, consumers, government and pharmaceutical industry with the objective of attaining wider agreement on these recommendations.

Results

The workshop involved 56 participants from Australia, New Zealand, Europe and North America. The following recommendations achieved consensus (>80% agreement from attendees) during the workshop via electronic voting:

Recommendation 1

Using estimated glomerular filtration rate (eGFR) via the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation[3] to guide the assessment of kidney function, except when directly measured glomerular filtration rate is clinically necessary.

eGFR was the preferred assessment method for the following reasons[4]:

- accounts for the standardisation of the creatinine assay (unlike the Cockcroft-Gault equation)
- more precise than other methods of kidney function estimation
- tested in a diverse range of populations
- easily available at point of care due to automatic reporting in lab test results.

Consideration of alternative assessment may be required in clinical situations where eGFR is less reliable, e.g. rapidly changing kidney function, extremes of body composition, fluid overload, dehydration, conditions of skeletal muscle, paraplegia, amputees.[5]

Recommendation 2

Where the anticancer drug dose is dependent on kidney function, eGFR using the CKD-EPI equation is suggested to guide dosing.

Kidney function should be used in conjunction with assessment of comorbidities, concomitant nephrotoxic drug exposure and clinical status of the patient when prescribing renally dependent anticancer drugs. Consider an alternative method for patients whose eGFR is borderline for clinical decision-making especially with platinum drugs, high-dose methotrexate, extremes of body composition or other clinical situations where eGFR is not as reliable.

Recommendation 3

The internationally accepted KDIGO chronic kidney disease categories[6] are suggested to guide stepwise dose adjustments of anticancer drugs in kidney dysfunction.

There may be limited studies to assess the application of KDIGO categories (Table 1) in dose adjustment of anticancer drugs in this guideline, however, the standardisation of kidney dysfunction classification across clinical practice reduces complexity of kidney function estimation and promotes uniformity with measurement.

Conclusion

eGFR using the CKD–EPI equation is the most accurate and convenient method for assessing kidney function in diverse populations (including cancer patients) and accounts for the standardisation of the creatinine assay.

This standardised approach reduces complexity of kidney function estimation, promotes uniformity of measurement and informs dosing calculations, to encourage consistency and safer delivery of anticancer treatment.

The consensus on the approach to assess and categorise kidney function provides a basis for formulating the dose adjustment recommendations in ADDIKD.

Table 1. KDIGO kidney function categories based on measured/estimated GFR[6]

GFR stage	GFR (mL/min/1.73 m²)	Description of kidney function
G1	≥90	Normal or high GFR
G2	60-89	Mildly decreased GFR
G3A	45-59	Mildly-moderately decreased GFR
G3B	30-44	Moderately-severely decreased GFR
G4	15-29	Severely decreased GFR
G5	<15	Kidney failure without kidney replacement therapy
G5D	<15	Kidney failure with kidney replacement therapy

Authors: Geeta Sandhu[a], Josephine Adattini[a], Niamh O'Neill[a], Evangeline Armstrong Gordon[a], Aisling Kelly[a], Julia Shingleton[a], Robyn Ward[a,b] and the International Working Party for the Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction.

a eviQ, Cancer Institute NSW, St Leonards, NSW, Australia
b Faculty of Medicine and Health, The University of Sydney, Camperdown, NSW, Australia

References:

1. Cockcroft D, Gault M. Prediction of creatinine clearance from serum creatinine. Nephron.1976;16(1):31-41.
2. National Health and Medical Research Council. Guidelines for guidelines, 2018 Available from: nhmrc.gov.au/guidelinesforguidelines.
3. Levey AS, Stevens LA. Estimating GFR using the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation: more accurate GFR estimates, lower CD prevalence estimates, and better risk predictions. Am J Kidney Dis. 2010; 55(4): 622-7.
4. 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
5. 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
6. 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).