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Letter comments on: Glomerular filtration rate estimation for carboplatin dosing in patients with gynaecological cancers

We congratulate Samani and colleagues[1] on their work investigating carboplatin dosing strategies using different glomerular filtration rate (GFR) estimation formulae. Their survey highlights significant differences in practice suggesting urgent need for standardisation. The gold standard nuclear medicine (NM)-measured GFR is impractical for many centres and most use formulae to estimate GFR. Samani et al. showed that the Cockcroft and Gault formula with weight adjustment (AdBW C&G) or the Cambridge GFR estimation formula version 2 (CamGFRv2) has the highest correlation with measured GFR and that the Wright and C&G without weight adjustment formulae are inaccurate. Overall, these findings suggest adoption of one of these methods of GFR calculation with area under the curve 5 (AUC5) dosing.[1]

To facilitate weight adjusted dosing in obese patients, our local guidelines changed from Wright AUC5 to C&G area under the curve 6 (AUC6) with maximum body weight adjustment (MBW C&G) in patients with a body mass index (BMI) >30 kg/m^2. The adoption to AUC6 was based on the protocols of national trials.[2-4] To investigate the effect of this change we undertook a retrospective review of all patients in NHS Greater Glasgow and Clyde (Scotland, UK) who were treated between 1 March 2018 to 31 August 2018 (Wright AUC5 protocol) and 1 October 2019 to 1 August 2020 (MBW C&G AUC6 protocol). All patients who received carboplatin Wright AUC5 or C&G AUC6 containing regimen for first-line ovarian cancer treatment were identified. Carboplatin dose, height, weight, baseline creatinine and pre-cycle 2 haematological results were collected. Administered doses were compared with the theoretical banded doses calculated using AdBW C&G AUC5 and CamGFRv2 AUC5.

A total of 58 patients were identified for the study: $n = 30$ Wright AUC5 and $n = 28$ MBW C&G AUC6. This cohort only had 11 patients with a BMI above 30 kg/m^2 ($n = 6$ in Wright

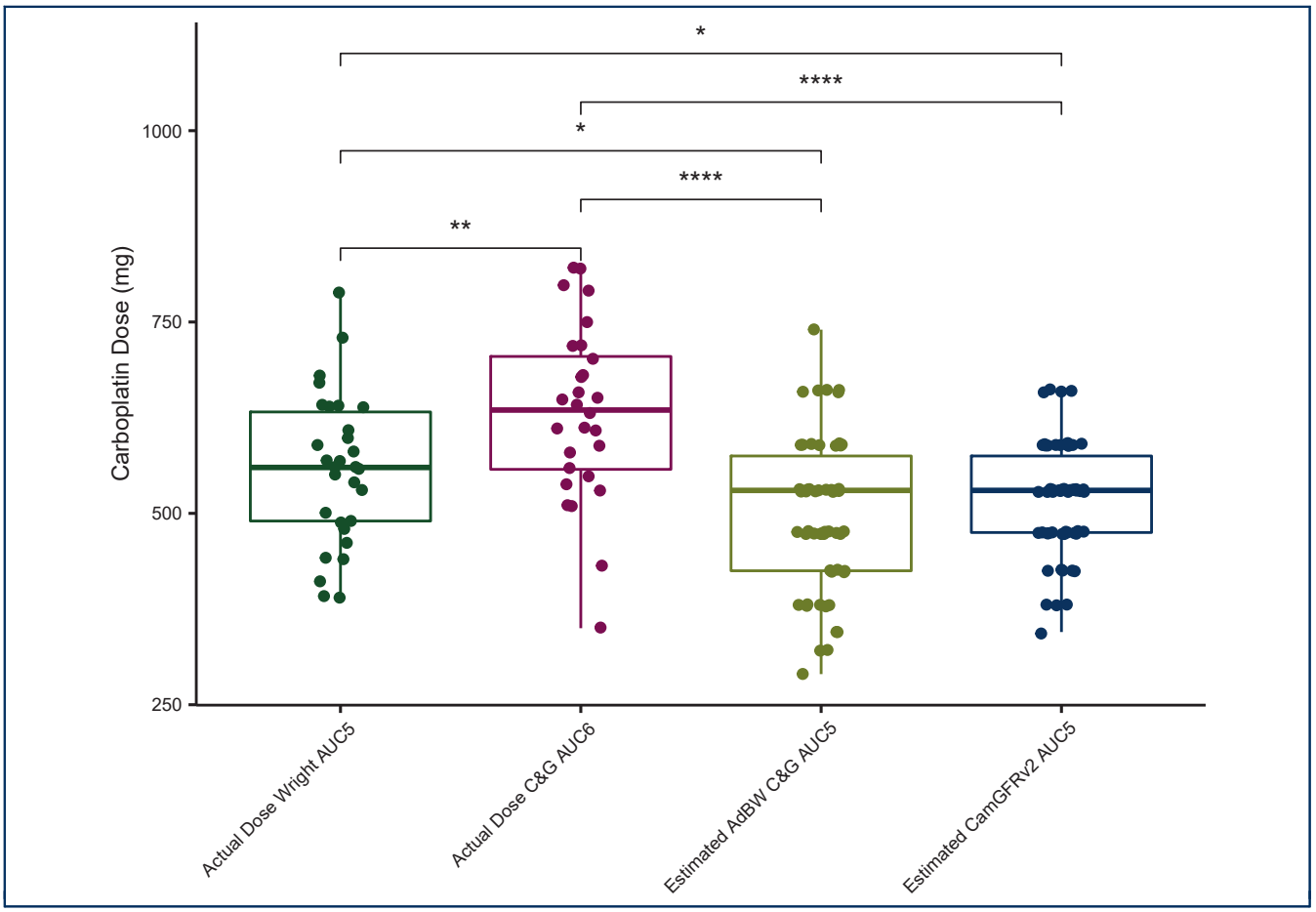

Figure 1. Comparison of carboplatin doses. Differences between actual carboplatin doses given based on two different GFR estimations and the estimate doses based on two new GFR estimation formulae (AdBW C&G and CamGFRv2). The Student's *t*-test statistical test was applied, with significance defined as $P < 0.05$ (* <0.05, ** <0.01, **** <0.0001).

AUC, area under the curve; C&G, Cockcroft and Gault formula; AdBW C&G, Cockcroft & Gault formula with weight adjustment; CamGFRv2, Cambridge GFR estimation formula version 2; GFR, glomerular filtration rate.

and $n = 5$ C&G). There were no significant differences between the two groups in age, height, weight, and creatinine. There was a 75-mg increase in the median dose given when we moved to the AUC6 C&G (560 mg Wright versus 635 mg C&G, Student's *t*-test $P = 0.011$). We did not see an increase in precycle 2 rates of haematological toxicities, in the context of this small sample, with the increase in carboplatin dose.

We applied the AdBW C&G and CamGFRv2 formulae to our cohort (Figure 1). Compared with actual doses administered, only 15 (26%) were within 10% when calculated using AdBW C&G AUC5 and 22 (38%) using CamGFRv2 AUC5. Both methods would have reduced the dose in most patients, with the largest difference in those who were administered C&G AUC6 regimens (median dose: C&G AUC6 635 mg, Wright AUC5 560 mg, calculated AdBW C&G 530 mg, calculated CamGFRv2 530 mg). This is in keeping with the findings of Samani et al.

A theoretical 'correct' dose gives optimal efficacy-to-risk ratio. Neither our study nor that of Samani et al. relate doses to survival outcomes. Previous trials allowed a range of dose calculating methods and no universally agreed method exists.[2-4] It is clear that raised BMI affects traditional GFR calculation methods and with rising obesity rates this is an issue.[5] The estimated GFR measurement should be as close to NM-measured GFR, so based on the data of Samani et al., we will adopt the AdBW C&G or CamGFRv2 methods described.[1]

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