

- Anderson, B.J. & Holford, N.H. Mechanism-based concepts of size and maturity in pharmacokinetics. *Annu. Rev. Pharmacol. Toxicol.* **48**, 303–332 (2008).
- Mathijssen, R.H., de Jong, F.A., Loos, W.J., van der Bol, J.M., Verweij, J. & Sparreboom, A. Flat-fixed dosing versus body surface area-based dosing of anti-cancer drugs in adults: does it make a difference? *Oncologist* **12**, 913–923 (2007).
- Rosner, G.L. *et al.* Relationship between toxicity and obesity in women receiving adjuvant chemotherapy for breast cancer: results from cancer and leukemia group B study 8541. *J. Clin. Oncol.* **14**, 3000–3008 (1996).
- Li, J. *et al.* CYP3A phenotyping approach to predict systemic exposure to EGFR tyrosine kinase inhibitors. *J. Natl. Cancer Inst.* **98**, 1714–1723 (2006).

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## Response to “Influence of Lean Body Weight on Anticancer Drug Clearance”

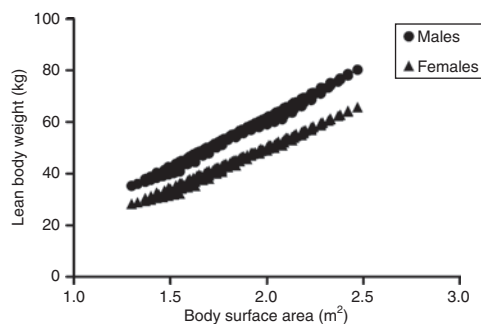
PY Han<sup>1</sup>, SB Duffull<sup>1,2</sup>,  
CMJ Kirkpatrick<sup>1</sup> and B Green<sup>1</sup>

**To the Editor:** In their letter, Mathijssen and Sparreboom report that the correlation between lean body weight (LBW, as defined by Janmahasatian *et al.*<sup>1</sup>) and clearance (CL) was no stronger than that between body surface area calculated using actual body weight (BSA<sub>ABW</sub>) and CL for a range of anticancer drugs.<sup>2</sup> This analysis was conducted on data gained from a previous study by Sparreboom *et al.*<sup>3</sup>

Their results highlighted the fact that the values of CL for all the anticancer drugs investigated were greater in obese patients than in lean patients and that these values, when normalized to

BSA<sub>ABW</sub> were not significantly different between obese and lean patients.<sup>3</sup> The first of these observations agrees with the first condition of our hypothesis, which states that CL is greater in obese patients than in nonobese ones.<sup>4</sup> The second observation aligns with our third condition, namely, that CL is linearly related to LBW.<sup>4</sup> We make this latter observation in the light of the fact that BSA<sub>ABW</sub> is highly correlated with LBW over the range of weight and height measurements in these analyses (Figure 1).

In their letter,<sup>2</sup> Mathijssen and Sparreboom concluded that LBW does not provide an added advantage over conventional size metrics (such as BSA<sub>ABW</sub>) when describing the CL of a range of anticancer drugs (those studied in ref. 3). However, it is important to note that either LBW or BSA<sub>ABW</sub> was the best descriptor of CL in seven of the eight anticancer drugs investigated in this analysis. Given that LBW and BSA<sub>ABW</sub> provide similar size relationships over the weight and height values in these studies, it would be difficult, and perhaps irrelevant, to attempt to distinguish between these size descriptors. However, it seems reasonable to consider size



**Figure 1** Relationship between lean body weight (LBW) and body surface area calculated using actual body weight (BSA<sub>ABW</sub>). Values of LBW and BSA<sub>ABW</sub> were calculated for patients of 40–120 kg and 150–190 cm.

descriptors that have a strong mechanistic background (such as LBW, which takes into account changes in body composition caused by obesity) over those that were determined for other purposes and empirically applied to pharmacokinetic studies.

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### CONFLICT OF INTEREST

The authors declared no conflict of interest.

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- Janmahasatian, S., Duffull, S.B., Ash, S., Ward, L.C., Byrne, N.M. & Green, B. Quantification of lean bodyweight. *Clin. Pharmacokinet.* **44**, 1051–1065 (2005).
- Mathijssen, R.H.J. & Sparreboom, A. Influence of lean body weight on anticancer drug clearance. *Clin. Pharmacol. Ther.* (2008), this issue.
- Sparreboom, A. *et al.* Evaluation of alternate size descriptors for dose calculation of anticancer drugs in the obese. *J. Clin. Oncol.* **25**, 4707–4713 (2007).
- Han, P.Y., Duffull, S.B., Kirkpatrick, C.M. & Green, B. Dosing in obesity: a simple solution to a big problem. *Clin. Pharmacol. Ther.* **82**, 505–508 (2007).

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