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REPLY

Appropriate chemotherapy dosing in obese patients with cancer

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We would like to thank Alessandro Laviano and colleagues for their correspondence on our Review article (Chemotherapy dosing in overweight and obese patients with cancer. *Nat. Rev. Clin. Oncol.* **10**, 451–459; 2013),[1] which raised some important issues on the effect of sarcopenia on chemotherapy-related toxicity in obese patients with cancer (Sarcopenia and chemotherapy dosing in obese patients. *Nat. Rev. Clin. Oncol.* doi:10.1038/nrclinonc.2013.108-c1).[2] Although the ASCO clinical practice guidelines on chemotherapy dosing in obese and overweight patients with cancer are based on an exhaustive review of the available clinical literature,[3] we acknowledge the complexity of the methods used to measure obesity, as well as the controversy surrounding the definition of obesity.[3,4] It should be made clear that, when referring to weight-based dosing, we (and the guideline panel) do not suggest the use of weight alone for calculating chemotherapy dosing in adults. Instead, actual body weight should be used in the calculation of body surface area, which is then used to estimate appropriate chemotherapy dose. The actual measurement of body composition requires sophisticated technology unfamiliar to practicing oncologists and is, therefore, generally not considered in clinical practice.

The prevalence and impact of sarcopenic obesity in patients with cancer clearly needs further investigation. However, a consistent lack of excess toxicity from chemotherapy has been observed in overweight and obese patients who lack other comorbidities and receive full-dose chemotherapy. Thus, the primary recommendation of the guideline panel is to avoid arbitrary dose reductions in these patients based on fear of excess toxicity. The panel recommends that chemotherapy dose and schedule modifications should be similar to those pursued in otherwise healthy weight patients receiving chemotherapy. An additional systematic review of the literature evaluating the toxicity or survival in obese and healthy weight patients receiving cancer chemotherapy has recently been published.[5] In this study, which analysed 12 studies and included >9,000 patients with cancer, the investigators found the same or lower rates of toxicity in obese patients with cancer compared with healthy weight individuals with cancer dosed on the basis of actual body weight. Importantly, no difference in overall survival was observed between obese and overweight patients receiving full-dose chemotherapy in this analysis compared with healthy weight individuals with cancer.[5] In an additional study of 247 patients receiving induction chemotherapy for acute myeloid leukaemia who were dosed on the basis of actual body weight, no differences were observed in days to neutrophil recovery, duration of hospitalization, infection or other toxicities between obese patients and healthy weight patients.[6] We agree with Laviano *et al.*[2] that additional studies of chemotherapy dosing considering fat-free mass and the issue of sarcopenic obesity are warranted and might further improve our ability to tailor appropriate chemotherapy dosing in this population. Nevertheless, the study by Prado *et al.*[7]—which reviews the current evidence on sarcopenic obesity and is cited in the correspondence[2]—highlights the wide heterogeneity and inconsistency of criteria applied to the classification of sarcopenic obesity and its association with disease risk. The relevance of the apparent association between sarcopenia with the pharmacokinetics and dose-limiting toxicities of the tyrosine kinase inhibitor sorafenib in patients receiving myelosuppressive chemotherapy is also unclear.[8]

Although we are sympathetic to the suggestion by Laviano *et al.*[2] that body composition analyses should be included in the assessment of patients with cancer when they begin chemotherapy, the additional requirements that this places on patients, clinicians and clinical investigators might prove to be problematic and could further decrease the already poor rates of accrual to cancer clinical trials. Even more problematic is the inaccuracy and cost of the available tools for measuring body composition,[2,9] as acknowledged by the authors.[2] The suggestion that whole-body CT scans be used for this purpose is intriguing, but would require high-resolution imaging, which is rarely used in cancer staging, and comes at a time of increasing concern about the long-term cancer risk in individuals exposed to radiation from CT imaging. Nevertheless, we agree that further retrospective and prospective clinical studies of new imaging modalities to assess body composition (including muscle mass) during chemotherapy could be very enlightening. At the same time, routine nutritional assessment and management of patients with cancer at all stages of their disease—before, during and after treatment—remains an important component of optimal cancer care.

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Competing interests
G. H. Lyman is co-chair and A. Sparreboom is a member of the ASCO Expert Panel involved in formulating the guidelines on appropriate chemotherapy dosing for obese adult patients with cancer.

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