letters to the editor

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Capecitabine dosing is not yet optimized for breast cancer

We read with interest the review by Zielinski et al. [1] regarding the optimal use of capecitabine and we agree that the dosing recommended on the package insert is not ideal for most patients. However, we are not satisfied that the existing studies have been designed to properly address the question and we do not believe that starting at a lower dose and using the 14/7 schedule should constitute the last word on this topic. For example, while noting our team’s development of the 7/7 schedule, a critical distinction was overlooked: this schedule was not empiric but was instead developed using a mouse model and mathematical methods of experimental design and analysis. Based on these data, we conducted a phase I study followed by phase II studies demonstrating the feasibility and safety of adding bevacizumab or lapatinib depending on human epithelial growth factor 2 status [2–4]. In addition, we demonstrated that body surface area-based dosing for capecitabine may not be necessary, as has been long recognized across the spectrum of cytotoxic agents [5]. This is of more than academic concern as the lower starting dose of capecitabine that the authors advocate using has been found, despite modest evidence of superiority in the metastatic setting, to be clearly inferior to either cyclophosphamide, methotrexate and 5-fluorouracil or Adriamycin (doxorubicin) and cyclophosphamide as adjuvant treatment [6].

Capcitabine dosing is particularly important given the potential utility of this agent in low- and middle-income countries where palliation of hormone-non-responsive breast cancer can be challenging and properly dosed capcitabine can offer the advantage of low risks of neutropenia, alopecia, and other troublesome or dangerous toxic effects. However, the only way for us to truly optimize the use of capcitabine and other important agents is to conduct scientifically designed, prospective, definitive phase III trials.

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