We thank Drs Hudis, Traina and Norton for their interest in our article. We are all in agreement that optimally dosed capecitabine offers important safety advantages over other chemotherapy options and that a randomized trial comparing capecitabine regimens would be the most appropriate way to identify the optimal dose. However, the feasibility of such a trial when there are arguably more pressing questions to answer in randomized trials is problematic.

While the authors’ carefully designed 7/7 regimen is of interest and has shown promising activity, the available data from small single-arm phase II studies (25 patients treated with capecitabine 7/7 plus bevacizumab; 11 patients treated with capecitabine 7/7 plus lapatinib) [1, 2] provide less robust information than those derived from large, randomized phase III trials of capecitabine 1000 mg/m² twice daily, such as RIBBON-1 (with bevacizumab) [3] and EGF100151 (with lapatinib) [4]. Furthermore, we note that despite the meticulous design of the regimen, 16 (64%) of 25 patients receiving capecitabine 7/7 plus bevacizumab nevertheless
required capcitabine dose delay or modification, 15 of these for grade 2 or 3 hand–foot syndrome. Thus, it appears that refinement of the regimen may still be necessary.

With reference to the CALGB 49907 trial [5], perhaps a more appropriate interpretation of the findings is that combination chemotherapy (which was anthracycline-based in 56% of patients) is more effective than six cycles of capcitabine monotherapy in the adjuvant setting. While the capcitabine arm was clearly inferior in this study, this is not surprising given the body of evidence showing greater efficacy with combination therapy versus monotherapy. Thus, our conclusion from the study is that if adjuvant anthracycline-based therapy is feasible and tolerable, this should be the preferred approach in patients ≥65 years of age. Meanwhile, randomized trials in both the neoadjuvant and the adjuvant settings have shown the benefit of integrating capcitabine (at doses lower than the registered dose) into combination regimens for early breast cancer [6, 7].

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references


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