In a recent commentary (1), Hertz and Rae have put the relevance of pharmacokinetically guided dosing of tamoxifen into perspective. We appreciate this effort and fully agree that more evidence is required to refine the relationship between exposure to the active tamoxifen metabolite endoxifen and clinical outcome parameters. On the basis of the relatively long survival of adjuvantly treated breast cancer patients, obtaining the highest level of evidence may take many years of further research, if feasible at all. However, this does not mean that based on the current evidence, including the recent work by Fox and colleagues (2), individual patients could not already benefit from systemic endoxifen concentration measurements. Of course, a threshold for efficacy has not been confirmed prospectively yet, but this does not mean that we should ignore extreme (low) endoxifen plasma concentrations. For instance, if the concentration has been measured and it is far below the currently adopted minimum value for efficacy of approximately 6 ng/mL (3), we feel it is unethical to not intervene and try to increase the exposure above this value, instead of just “waiting” for a potential recurrence. From daily clinical practice, we know that patients are highly motivated to know their endoxifen levels, despite all reservations regarding its interpretation. We agree that endoxifen levels must be measured by a certified laboratory. With multiple reports of validated endoxifen analytic assays available, we believe this is manageable for most laboratories experienced in therapeutic drug monitoring.

In the second part of their commentary, Hertz and Rae (1) proposed an individualized dosing algorithm for tamoxifen treatment. On the basis of clinical parameters and CYP2D6 phenotype, the starting dose is determined and then, after a month, dosing is adjusted on the basis of the actual drug exposure. This is an option, as also the use of a dextromethorphan phenotyping test for endoxifen exposure is a possible tool to determine a tailored starting dose for the individual patient (4). Despite the comprehensiveness of their algorithm, this model lacks a major factor in dose individualization, that is, the continuing change in exposure over time. Several factors have been mentioned to predict endoxifen exposure before treatment initiation, but concomitant medication, complementary and alternative medicine, and adherence, for example, might change during treatment (5). Therefore, systemic drug exposure may also be influenced considerably later on during treatment, and it is vital to follow-up exposure over time, especially as tamoxifen treatment can comprise many years.

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

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Individualized Tamoxifen Dose Escalation—Letter

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