Letter to the Editor

Clinical Cancer Research

FDG PET and FES PET Predict PFS on Endocrine Therapy—Letter

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With great interest, we read the article by Kurland and colleagues (1) that investigates the value of ^{18}F-fluoroestradiol (FES) and ^{18}F-fluorodeoxyglucose (FDG) PET for the prediction of progression-free survival (PFS) in 84 patients with advanced, estrogen receptor (ER)–positive breast cancer treated with endocrine therapy. The PET scans were performed prior to (change of) endocrine treatment. The authors concluded that tumor FES uptake alone was not correlated with PFS. Yet, in a small subgroup of patients with high tumor FDG uptake, low FES uptake predicted poor PFS (3.3 vs. 7.9 months).

These conclusions warrant additional discussion, as they are not in line with several previous trials showing that FES uptake predicts response to endocrine treatment (2). In the current study, the authors did not report the extent of prior endocrine treatments. We wonder whether extensive pretreatment could have caused these conflicting results. ER expression is a prerequisite for benefit to endocrine therapy. However, endocrine resistance has multiple mechanisms besides the loss of or mutations in the ER, such as upregulation of other signaling transduction pathways and altered expression of coregulatory proteins and miRNAs (3). These mechanisms, which can be evoked by inhibition of the ER pathway with (multiple lines of) endocrine treatment, will not prevent the binding and internalization of FES per se and could explain the contrasting results between FES PET and clinical outcome found by Kurland and colleagues. Nonetheless, FES PET can still have meaningful clinical utility by evaluating the presence and extent of ER expression across tumor lesions within a patient with newly or progressed breast cancer, as receptor conversion has been reported in 14% to 40% of the patients (4).

An additional point for discussion is the quantification analysis, as it is not clear why only $\leq$3 lesions with the highest SUV_{max} were evaluated. We previously reported that interlesional heterogeneity of FES uptake on whole-body static PET/CT is present and correlates with representative biopsies (5). By not taking heterogeneity into account, this could inadvertently have added to the contrasting results between FES PET and clinical outcome, as patients could have progressive disease based on growth of these unevaluated FES-negative, endocrine-resistant lesions.

We hope the authors can elaborate whether correcting for prior endocrine treatment and evaluating FES-negative lesions could improve the value of FES PET for the prediction of PFS on endocrine therapy in patients with breast cancer.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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