18F-FDG PET/CT for Early Prediction of Response to Neoadjuvant Lapatinib, Trastuzumab, and Their Combination in HER2-Positive Breast Cancer: Results from Neo-ALTTO


Summary:
- Anti-HER2+ neoadjuvant Tx monitored by PET at baseline, and at 2 weeks and 6 weeks post Tx.
- Complete response to Tx was 2x higher for PET responders than PET non-responders.
- Early imaging assessment with PET can identify patients with increased likelihood of complete response after neoadjuvant chemo.

Abstract
Molecular imaging receives increased attention for selecting patients who will benefit from targeted anticancer therapies. Neo-ALTTO (Neoadjuvant Lapatinib and/or Trastuzumab Treatment Optimisation) enrolled 455 women with invasive human epidermal growth factor receptor 2 (HER2)–positive breast cancer and compared rates of pathologic complete response (pCR) to neoadjuvant lapatinib, trastuzumab, and their combination. Each anti-HER2 therapy was given alone for 6 wk, followed by 12 wk of the same therapy plus weekly paclitaxel. The early metabolic effects of the anti-HER2 therapies on the primary tumors and their predictive values for pCR were assessed in a subset of patients.

Methods: Eighty-six patients underwent 18F-FDG PET/CT at baseline and weeks 2 and 6 of anti-HER2 treatment. An imaging core laboratory provided central validation, and 2 independent reviewers, masked to assigned treatment arm and clinical outcomes, performed consensus 18F-FDG PET/CT readings. Maximum standardized uptake value (SUVmax) reductions from baseline were used to measure metabolic response.

Results: Seventy-seven of the 86 enrolled patients presented an evaluable baseline 18F-FDG PET/CT scan; of these, 68 and 66 were evaluable at weeks 2 and 6, respectively. Metabolic responses in the primary tumors were evident after 2 wk of targeted therapy and correlated highly with metabolic responses at week 6 ($R^2 = 0.81$). pCRs were associated with greater SUVmax reductions at both time points. Mean SUVmax reductions for pCR and non-pCR, respectively, were 54.3% versus 32.8% at week 2 ($P = 0.02$) and 61.5% versus 34.1% at week 6 ($P = 0.02$). 18F-FDG PET/CT metabolic response rates at weeks 2 and 6 were 71.6% and 60%, respectively using European Organization for Research and Treatment of Cancer criteria; pCR rates were twice as high for 18F-FDG PET/CT responders than nonresponders (week 2: 42% vs. 21%, $P = 0.12$; week 6: 44% vs. 19%, $P = 0.05$).

Conclusion: Early metabolic assessment using 18F-FDG PET/CT can identify patients with an increased likelihood of pCR after neoadjuvant trastuzumab, lapatinib, or their combination when given with chemotherapy.