[^{11}C]-Vorozole PET as a Predictive Imaging Biomarker of Aromatase Inhibitor Resistance in Postmenopausal ER-positive Breast Cancer

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Background

- Aromatase inhibitors (AIs), such as letrozole and vorozole, block the final step of estrogen biosynthesis and have been associated with improved survival outcomes in postmenopausal women with hormone receptor - positive breast cancer (BC).
- Prior studies have validated the utility of [^{11}C]-Vorozole PET imaging in detecting aromatase expression in vivo in aromatase-expressing breast tumors.

Aims

- To investigate the differences in aromatase expression in affected and non-affected breasts between ER-positive (ER+) and ER-negative (ER-) patients at baseline and following letrozole administration
- The correlations between changes in [^{11}C]-Vorozole PET signal and clinical outcomes.

Methods

- Nineteen postmenopausal women were enrolled.
- Clinicopathological characteristics and prior AI treatment history were extracted from the electronic medical record.
- Continuous variables were compared using the Wilcoxon rank-sum test, and correlations were assessed using Spearman's rank correlation coefficient.
- A two-sided p-value < 0.05 was considered statistically significant.

Methods (cont.)

Baseline [^{11}C]-Vorozole PET imaging

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Same day single 2.5mg dose of Letrozole

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Repeat [^{11}C]-Vorozole PET two hours post Letrozole

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Mean standardized uptake values (SUVs) were measured at baseline and after letrozole administration in regions of interest including the bilateral breasts and thoracic spine

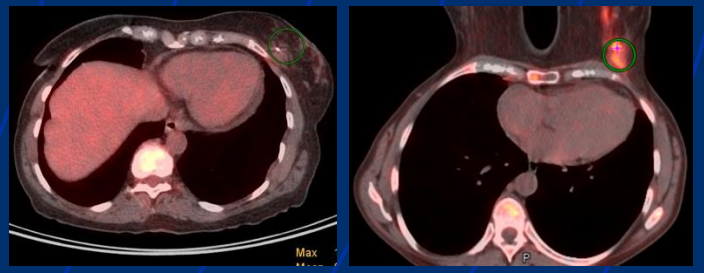
Results

- SUV signals in diseased and healthy breasts were not significantly different in either ER+ or ER- patients at baseline or after letrozole.
- SUV suppression ranged from-25.8% to 49.6% in the diseased breast following letrozole intake.
- There was no difference in SUV signal in the whole thoracic spine between patients with and without metastases, but most biopsy-confirmed vertebral metastatic lesions presented high [^{11}C]-Vorozole signal.
- Among ER+ patients with concurrent FDG-PET, signal distribution was largely concordant between FDG-PET and [^{11}C]-Vorozole PET.

Results (cont.)

- Some FDG-negative lesions showed positive [^{11}C]-Vorozole uptake and were confirmed malignant by pathology (Figure below).
- Patients with increased [^{11}C]-Vorozole uptake post-letrozole had a shorter average time to progression than those with decreased signal (20.9 vs. 30.4 months), though this difference did not reach statistical significance (P=0.63).

^{18}F-FDG | ^{11}C-Vorozole



Conclusion

- [^{11}C]-Vorozole PET demonstrated higher sensitivity than FDG-PET in detecting certain metastatic lesions.
- An increase in [^{11}C]-Vorozole uptake following letrozole administration may signal resistance to AIs given unsuppressed aromatase expression and correlate with shorter progression-free survival.
- [^{11}C]-Vorozole PET has potential as a predictive imaging biomarker to identify patients who may benefit from early alternative treatments such as fulvestrant.