Letter to the Editor

PET/CT in Locally Advanced Breast Cancer: Time for a Guideline Change?

Re: Hyland CJ, Varghese F, Yau F, et al. Use of 18F-FDG PET/CT as an initial staging procedure for stage II–III breast cancer: a multicenter value analysis. *J Natl Compr Canc Netw* 2020;18(11):1510–1517.

We read with interest the article by Hyland et al,¹ in which 564 complete records of breast cancer patients with clinical stage II–III disease, who initiated screening for the I-SPY2 trial at 4 institutions, were reviewed to compare staging with FDG-PET/CT versus standard of care (SoC). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Breast Cancer recommend considering CT of the chest, abdomen ± pelvis, and bone scan in appropriate patients.² At this time, the NCCN Guidelines do not recommend FDG-PET/CT, but state that “FDG-PET/CT may ... be helpful in identifying unsuspected regional nodal disease and/or distant metastases when used in addition to standard imaging studies.” In the multicenter study by Hyland et al,¹ PET/CT reduced false-positive risk by half and decreased workup for incidental findings, allowing for earlier treatment start. PET/CT was cost-effective, and at one institution was shown to be cost-saving. The de novo metastatic disease rate was 4.6%. However, the authors offer no results by stage or tumor/node combination to help clinical decisions. In another recent study published in *JNCCN*,³ among 196 patients with breast cancer, the overall upstaging rate to stage IV based on findings of unsuspected distant metastases was 14% (n=27), including 0% for stage IIA, 13% for stage IIB (10/79), 22% for stage IIIA (9/41), 17% for stage

IIIB (5/30), and 37% for stage IIIC (3/8). PET/CT had comparable costs than SoC and had lower radiation dose exposure.³ In another recent retrospective study, PET/CT demonstrated distant disease in 4.9% of 303 patients with stage I or II breast cancer, including 0.8% in stage IIA and 9.8% in stage IIB breast cancer.⁴ In a prospective study of 254 patients with breast cancer, we detected distant metastases with PET/CT in 2.3% of patients with stage IIA disease, and in 10.7% with clinical stage IIB disease.⁵ PET/CT had similar performances whatever the breast cancer subtype. Other studies also showed that PET/CT reveals distant metastases in 10% to 15% of patients with stage IIB disease, whatever the breast cancer subtype.⁵ Nodal metastases outside Berg-I/II levels should also be taken into account, identified with PET/CT, with impact on management.^{5,6}

The 2 recent manuscripts in *JNCCN* add financial and radiation protection data to support the assertion that FDG-PET/CT should be used in patients with IIB–IIIC breast cancer. We hope this growing evidence will lead consensus guidelines to include FDG-PET/CT for the systemic staging of IIB–IIIC breast cancer at initial diagnosis.

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Authors' Reply

To the Letter to the Editor by Groheux et al

The recent articles by Ko et al¹ and our group² contribute to the growing consensus that 18F-FDG PET/CT adds value to the care of locally advanced breast cancer. Retrospective and prospective evidence suggests that 18F-FDG PET/CT detects unsuspected axillary and distant metastases in a sizable proportion of patients, with detection rate increasing by stage.^{3–5} 18F-FDG PET/CT is both more sensitive and specific than conventional imaging (CT +

bone scan) in this patient population.^{2,5–7} Identification of distant metastatic disease directly affects management, potentially preventing costs, morbidity, and emotional burden associated with inappropriate treatments. In the ECOG-ACRIN E2108 trial, no survival benefit was observed in patients with de novo stage IV breast cancer randomized to surgery for locoregional control after a course of systemic therapy.⁸ Although some patients still opt to proceed

with surgery in the setting of stage IV disease, recognition of distant metastases may lead some to revise their surgical preferences. Furthermore, in known stage IV disease, oncologists may opt to refrain from recommending chemotherapy with the goal of cure and are more likely to recommend a hormone-based therapy regimen, particularly for older patients or those with minimal visceral disease. Conversely, data from the phase II SABR-COMET trial