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NCCN Guidelines Panel: Breast Cancer

On behalf of *Zionexa*, I respectfully request the *NCCN Breast Cancer Panel* to review the enclosed data for inclusion of *FES PET (Cerianna™)* in the evaluation of ER status in patients with recurrent and/or metastatic breast cancer.

Specific Changes: We respectfully suggest the following revisions and/or additions for NCCN consideration in the following sections:

1. BINV 17, RECURRENT/STAGE IV (M1) DISEASE
    a. In Workup, add "FES PET (optional)" after or in addition to "FDG PET (optional)"
        i. Include footnote: "In metastatic disease and failing hormonal treatment consider using FES PET to assess for ER status in metastatic lesions."
    b. In Workup, revise "Determination of tumor ER/PR and HER2 status on metastatic site" to "Determination of tumor ER/PR and HER2 status on metastatic site(s) by biopsy and/or adjunct functional imaging
        i. Include footnote: "In patients with multiple metastatic lesions, or, when biopsy cannot safely be obtained, FES PET may be considered to assess the ER status of these lesions noninvasively"
    c. In footnotes, revise "fff" to add: "FES PET may be considered to assess the ER status of lesions where biopsy is not feasible."
2. BINV 21, SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV (M1) DISEASE: ER- AND/OR PR-POSITIVE; HER2-NEGATIVE
    a. In footnote "eee", add "An alternative to empiric second line therapy is functional imaging with FES PET to determine ER status."
3. BINV 23, SYSTEMIC TREATMENT OF RECURRENT OR STAGE IV (M1) DISEASE: ER- AND/OR PR-POSITIVE; HER2-POSITIVE
    a. In footnote "eee", add "An alternative to empiric second line therapy is functional imaging with FES PET to determine ER status."
4. BINV-A (PAGE 2), PRINCIPLES OF BIOMARKER TESTING: HORMONE RECEPTOR TESTING
    a. Add as either separate additional bullet point or as footnote to the first bullet point or a footnote to the second bullet point: "FES PET may be considered as adjunct to pathology in recurrent/metastatic breast cancer to assess ER status of metastatic lesions to determine if a patient is a candidate (or continues to be a candidate) for endocrine therapies"
5. MS-51, Recurrent/Stage IV Breast Cancer: Staging and Workup for Recurrent and Stage IV Breast Cancer

a. Add to the Paragraph 5 "The NCCN Panel recommends that re-testing the receptor status of …" the following sentence "Although biopsy of metastatic sites to confirm receptor status is recommended, in patients in whom biopsy is not feasible, as an alternative to empiric hormonal therapy, functional imaging (FES PET) to determine ER status to optimize treatment may be considered. In patients with second or subsequent progression, where biopsy is not routinely performed, functional imaging (FES PET) to determine ER status to optimize treatment should be considered."

b. Add to the Paragraph 3 "The NCCN Panel recommends that metastatic disease at presentation or first recurrence…" the following sentence "FES PET may be considered to assess ER status of metastatic lesions that cannot be biopsied, or to assess bone lesions."

FDA Clearance:

FES (CERIANNA™) is approved by the FDA for the following indication:

CERIANNA™ is a radioactive diagnostic agent indicated for use with positron emission tomography (PET) imaging for the detection of estrogen receptor (ER)-positive lesions as an adjunct to biopsy in patients with recurrent or metastatic breast cancer.

Limitations of Use: Tissue biopsy should be used to confirm recurrence of breast cancer and to verify ER status by pathology. CERIANNA™ is not useful for imaging other receptors, such as human epidermal growth factor receptor 2 (HER2) and the progesterone receptor (PR).

Rationale:

As stated in current NCCN breast cancer guidelines, discordance of ER status between primary and metastatic tumors is known to occur in a significant number of cases (3.4-60%), and additionally, biopsy of a metastatic lesion, while recommended, is not feasible in some clinical situations[1–3]. FES is a synthetic estrogen analog that binds to estrogen receptors with high affinity and, when radiolabeled with Fluorine 18, allows visualization via PET imaging[4].

Multiple metaanalyses have reported sensitivity (0.82 to 0.86) and specificity (0.80 to 0.98) for detection of ER positive lesions by FES when compared to tissue reference assays[5]. As a complement to current tools (biopsy), FES PET can assess ER at more than a single location, is non-invasive, and can assess lesions that may be difficult to biopsy or low yield, such as lesions in the bone and brain[6,7].

Unlike traditional imaging tools (CT/MRI and FDG PET), which are used to locate lesions and stage disease, FES is a 'receptor imaging' agent, and plays a role closer to biopsy in characterizing known lesions by ER status, potentially further personalizing therapeutic decisions. ER discordance between metastatic lesions has been demonstrated in studies using FES PET with attendant therapeutic implications[8–12].

References:

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