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NCCN Guidelines Panel: Breast Cancer

Dear Panel Members,

On behalf of Foundation Medicine, I respectfully request the NCCN® Breast Cancer Guidelines Panel review the enclosed data supporting updates to the Guidelines and include validated next-generation sequencing (NGS) as a testing modality to evaluate eligibility for HER2-targeted therapies.

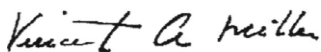
Specific Changes and Rationale: Include validated next-generation sequencing assays such as FoundationOne CDx™ in the “Principles of HER2 testing” (BINV-A) as an additional method to identify *HER2 (ERBB2)* amplification

- The FoundationOne CDx™ (F1CDx) assay is FDA-approved as a companion diagnostic test [1] to identify *HER2* amplification for selecting patients with breast cancer for treatment with HER2 targeted therapy including Herceptin® (trastuzumab), Kadcyla® (ado-trastuzumab-emtansine), or Perjeta® (pertuzumab).
- Clinical validity was established by a retrospective concordance study comparing results from the F1CDx assay against the FDA-approved HER2 FISH PharmDx® Kit (Dako Denmark A/S) as a reference standard [1]: the Positive Percent Agreement was 89.4% (101/113 reference *HER2* FISH-positive samples) and the Negative Percent Agreement was 98.4% (180/183 reference *HER2* FISH-negative samples).
- Concordance between F1CDx and HER2 FISH testing was greater than concordance between two replicate HER2 FISH tests [1].

FDA Approval: FoundationOne CDx is an FDA-approved (Class III) next generation sequencing based in vitro diagnostic device for detection of substitutions, insertion and deletion alterations (indels), and copy number alterations (CNAs) in 324 genes and select gene rearrangements, as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB) using DNA isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue specimens. The test is intended as a companion diagnostic to identify patients who may benefit from treatment with specific targeted therapies in accordance with the approved therapeutic product labeling. Additionally, F1CDx is intended to provide tumor mutation profiling to be used by qualified health care professionals in accordance with professional guidelines in oncology for patients with solid malignant neoplasms.

Thank you for your review of this submission.

Sincerely,



Vincent A. Miller, M.D.
Chief Medical Officer
Foundation Medicine

References

1. www.accessdata.fda.gov/cdrh_docs/pdf17/P170019C.pdf. (n.d.).