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NCCN Guidelines Panel: Pancreatic Cancer

Dear Panel Members,

On behalf of Foundation Medicine, I respectfully submit this late-breaking publication and request to the NCCN® Pancreatic Cancer Guidelines Panel for review.

Specific Changes and Rationale: **Add "comprehensive genomic profiling" to the initial work-up of a patient with locally advanced or metastatic pancreatic cancer (pages PANC-5 and PANC-7).**

Pishvaian, et al[1] recently published data demonstrating the clinical utility of comprehensive genomic profiling in patients with pancreatic cancer. Tumor samples were obtained from 640 patients and 50% of the patients had an actionable alteration; 27% of patients had a highly actionable alteration. Among patients with highly actionable biomarkers, those who received matched therapy (n=17) had a significantly longer median progression-free survival (PFS) than those who received unmatched therapy (n=18; PFS = 4.1 vs. 1.9 months; HR: 0.47; 95% CI: 0.24-0.94; adjusted *P*-value = 0.03). Additionally, of the patients with follow-up data, 21% (26/126) were enrolled in a clinical trial.

Consistent with this study, other reports have demonstrated clinical benefit to targeted therapy for patients with pancreatic cancer and tumors harboring actionable alterations, including tumors with microsatellite-High (MSI-High) status treated with anti-PD1 therapy [2], tumors with *BRCA1/2* or *PALB2* mutations treated with platinum-based chemotherapy or PARP inhibitor [3-6], tumors with *BRAF* mutation treated with MEK inhibitor [3], tumors with *HER2* amplification treated with HER2 targeted therapy [7], and tumors with *ALK*-fusion [8,9], *NTRK*-fusion[10], *RET* fusion [11], or *ROS1*-fusion[10] treated with matched tyrosine kinase inhibitors.

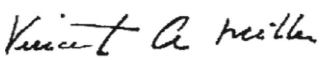
FDA Approval: FoundationOne *CDx*™ is an FDA approved (Class III) next generation sequencing based in vitro diagnostic device for detection of substitutions, insertion and deletion alterations (indels), and copy number alterations (CNAs) in 324 genes and select gene rearrangements, as well as genomic 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.

Metastatic disease is incurable and patients with pancreatic cancer require opportunities for genomically matched therapies and enrollment into clinical trials. Numerous promising therapeutic approaches are based upon genomic characterization of tumors and therefore many clinical trials require specified genomic alterations for patient enrollment, including trials offered by the NCI (NCI-MATCH) and ASCO (TAPUR). Consistent with the NCCN® recommendation to provide patients with opportunities to participate in therapeutic clinical trials, comprehensive genomic profiling assays like

FoundationOne *CDx*™, can potentially match more patients to targeted therapies in clinical trials based on detected alterations. Foundation Medicine has joined both the NCI-MATCH and ASCO TAPUR studies as an approved testing platform, and is accelerating accrual to these transformative trials using the combination of CGP and clinical trial matching capabilities. These data indicate that CGP is an essential addition to the clinical care of patients with this often-deadly malignancy.

Thank you for your review of this submission.

Sincerely,



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