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Date of request: November 6, 2020
NCCN Guidelines Panel: Ovarian Cancer

Dear Panel Members,

On behalf of Foundation Medicine, I respectfully request the NCCN® Ovarian Cancer Guidelines Panel consider the following updates pertaining to the evaluation and management of patients with ovarian cancer:

Requested Update and Rationale: Update "Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer" footnote 'z' (OV-6, OV-7); "Principles of Pathology" (OV-B 1 of 3); and "Principles of Systemic Therapy" (OV-C, 3 of 10) to indicate that *tumor molecular testing can be performed as part of a single, validated or FDA-approved, NGS-based broad molecular profiling tissue-based assay or liquid biopsy to inform patient treatment options, including clinical trials.*

On October 27, 2020 the FDA approved FoundationOne®Liquid CDx, a liquid biopsy comprehensive genomic profiling test, as a companion diagnostic for Rubraca®(rucaparib), for the treatment of adult patients with a deleterious *BRCA* mutation (germline and/or somatic)-associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with two or more chemotherapies.[1]

The clinical effectiveness of FoundationOne Liquid CDx as a companion diagnostic to identify patients with ovarian cancer harboring *BRCA1* or *BRCA2* alterations for treatment with rucaparib was demonstrated using pre- rucaparib treatment blood samples from the ARIEL2 study. ARIEL2 was a two-part, single-arm, open-label Phase 2 efficacy study of oral rucaparib in patients with relapsed high-grade serous or endometrioid epithelial ovarian, fallopian tube, or primary peritoneal cancer.[2] The bridging study was conducted to evaluate: 1) the concordance between *BRCA1* and *BRCA2* alteration status by the clinical trial tissue assay and FoundationOne Liquid CDx, and 2) the clinical efficacy of rucaparib treatment in patients that would be eligible for therapy based on *BRCA1* and *BRCA2* alteration status as determined by FoundationOne Liquid CDx.[3]

- The ARIEL2 study is complete and enrolled 491 patients. Pre-rucaparib treatment plasma samples were available for 55% (271/491) of patients dosed in ARIEL2. FoundationOne Liquid CDx data were available for 80% (217/271) of the patients with samples tested; 49 failures were due to insufficient remaining plasma volume or insufficient DNA extraction yield. The PPA and NPA between FoundationOne Liquid CDx and the CTA for detection of *BRCA1* or *BRCA2* alterations in the all patient population: PPA (95%CI): 93.8% (86.8%,100.0%) and NPA (95%CI): 97.4% (2.5%,100.0%)[3]
- Of 64 patients in the primary efficacy population, FoundationOne Liquid CDx results were available for 42% (27/64) and used for concordance and efficacy analyses. The concordance between FoundationOne Liquid CDx and the CTA for the detection of *BRCA1* or *BRCA2* mutations in the primary efficacy population was: PPA (95%CI): 100% (86.8%,100.0%) and NPA (95%CI): 100% (2.5%,100.0%).[3]
- The ORR in the primary efficacy population was 53.8% [33.4%-73.4%] in the *BRCA*-positive patients as determined by FoundationOne Liquid CDx, which is comparable to the ORR of 54.1%[40.8%-66.9%] in patients identified by the CTA. The median DOR was 225 days [115-403] in FoundationOne Liquid CDx *BRCA*-positive patients from the primary efficacy population. This is similar to the median DOR of 288 days [170-403] for the primary efficacy population in *BRCA*-positive patients by the CTA. The data provided demonstrated that FoundationOne Liquid CDx identified *BRCA*-positive ovarian cancer patients treated with rucaparib with an ORR and clinically meaningful DOR similar to that observed in the clinical study.[3]

FoundationOne CDx, a tissue-based broad companion diagnostic, is also FDA-approved for the identification of deleterious *BRCA* mutations for determining treatment of ovarian cancer with rubraca, as well as for olaparib.[4]

Thank you for your review of this submission.

Sincerely,

Brian Alexander, M.D.
Chief Medical Officer
Foundation Medicine Inc.

References:

1. FoundationOne Liquid CDx Technical Information. Accessed 11-5-2020 at: https://assets.ctfassets.net/w98cd481qyp0/3a8jFw3KUjIU3RWPdcT9Ax/4ab672fcebe60fdd480621d5d5499e36/FoundationOne_Liquid_CDx_Label_Technical_Info.pdf
2. Swisher EM, Lin KK, Oza AM, et al. Rucaparib in relapsed, platinum-sensitive high-grade ovarian carcinoma (ARIEL2 Part 1): an international, multicentre, open-label, phase 2 trial. *The Lancet Oncology.* 2017;18(1):75-87.
3. US Food & Drug Administration, Premarket Approval (PMA), FoundationOne Liquid CDx P200006, Summary of Safety and Effectiveness. Accessed 11-5-2020: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=p200006
4. FoundationOne CDx Technical Information. Accessed 11-5-2020 at: https://assets.ctfassets.net/w98cd481qyp0/41rJj28gFwtxCwHQxopaEb/2725881bbc67d6f323ab893851344c4a/FoundationOne_CDx_Label_Technical_Info.pdf