On behalf of Illumina, I respectfully request the NCCN Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer v3.2017 guideline panel to review the enclosed documents in support of including next-generation sequencing (NGS) when referring to various “molecular” related terminology and applications in the published guidelines as described in detail below.

Specific Requested Changes:
We propose changing “FDA-approved test” to “FDA-approved NGS-based test” and adjust “or other validated tests” to include “or other validated NGS-based tests”.

FDA Clearance:
The FoundationFocus™ CDx BRCA is the first NGS-based companion in vitro diagnostic device approved by the FDA (PMA P160018) for qualitative detection of BRCA1 and BRCA2 alterations in formalin-fixed paraffin-embedded (FFPE) ovarian tumor tissue. The FoundationFocus CDx BRCA assay detects sequence alterations in BRCA1 and BRCA2 (BRCA1/2) genes. If an ovarian cancer patient is positive for any of the deleterious alterations specified in the BRCA1/2 classification, the patient may be eligible for treatment with Rubraca™ (rucaparib), the second poly (ADP ribose) polymerase inhibitor (PARP inhibitor) to gain FDA approval for treating ovarian cancer.

Rationale:
As more data and techniques become available to evaluate patients’ gene mutations and tumor mutational profiles, a more prescriptive approach is needed to direct laboratories to the most clinically relevant techniques. The FDA-approved NGS companion diagnostic test for rucaparib can detect both germline and somatic BRCA1/2 mutations, which can help to identify up to twice as many patients who may benefit from this targeted therapy, compared to Sanger sequencing. NGS can more accurately and sensitively detect, using less FFPE tumor tissue, a broader range of BRCA-related mutations.

The current Ovarian NCCN guidelines (figure OV-B (5 of 8) and (6 of 8) footnote “o”) recommend for prescribing rucaparib, "For patients with deleterious germline and/or somatic BRCA mutated (as detected by an FDA-approved test or other validated test performed in a CLIA-approved facility) advanced ovarian cancer who have been treated with two or more lines of chemotherapy." To make a distinction between the FDA approved BRCA 1/2 Sanger sequencing assay, approved for detecting germline alterations in blood or saliva prior to prescribing Lynparza™ (olaparib) and the FDA approved NGS assay for detecting germline and somatic BRCA 1/2 mutations in FFPE tumor tissue, it would be accurate to specify an NGS-based test, as this type of test is required by the FDA.

Proposed Changes:
Figure Changes: OV-B (5 of 8) and (6 of 8) Footnote o:

Current: “For patients with deleterious germline and/or somatic BRCA mutated (as detected by an FDA-approved test or other validated test performed in a CLIA-approved facility) advanced ovarian cancer who have been treated with two or more lines of chemotherapy.”

Proposed: “For patients with deleterious germline and/or somatic BRCA mutated (as detected by an FDA-approved NGS-based test or other validated NGS-based tests performed in a CLIA-approved facility) advanced ovarian cancer which have been treated with two or more lines of chemotherapy.”
The following articles are submitted in support of using NGS as a technique to test molecular abnormalities. We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of some of these publications.


2) https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/209115s0001bl.pdf


Sincerely,
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