

Submitted by:

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NCCN Guidelines Panel: Ovarian Cancer

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On behalf of the Ovarian Cancer National Alliance and the community of survivors we represent, I respectfully request the NCCN Ovarian Cancer Guideline Panel to review the enclosed comments regarding their recent recommendation that ovarian cancer patients considering therapy with a PARP inhibitor be tested with any BRCA test, not exclusively the FDA-cleared or approved companion diagnostic. We strongly disagree with this recommendation as it may put patients at risk.

Specific Changes: Regarding footnote “g” in the list of acceptable recurrence therapies in version 2.2015, which states olaparib can be selected for patients “with deleterious germline BRCA-mutated (as detected by an FDA-approved test or other validated test performed in a CLIA-approved facility)”, **we recommend striking “or other validated test performed in a CLIA-approved facility”.**

FDA Clearance: The FDA has approved BRCAAnalysis CDx to assess whether a patient previously treated for ovarian cancer has a germ-line mutation in the *BRCA1/2* genes and may be a candidate for treatment with Lynparza (olaparib).

Rationale: With the recent approval of olaparib, a PARP inhibitor targeting *BRCA1/2* germline mutant related cancer cells, for the treatment of ovarian cancer, it is critical that all women diagnosed with ovarian cancer receive *BRCA1/2* testing with an FDA-cleared or approved companion diagnostic to determine their eligibility for olaparib, for several reasons that are outlined below:

- (1) By implying that FDA-approved and unregulated tests are equivalent, **NCCN is setting a dangerous precedent** that many public and private payers may follow. In fact, recently the Medicare contractor Palmetto released its “Response to Comments for MoIDX: BRCA1 and BRCA2 genetic testing” document, which cited the NCCN guidelines in their decision regarding which tests it would cover for olaparib selection.
- (2) The analytic and clinical utility of *BRCA1/2* testing offered in CLIA laboratories has not been established. When using a diagnostic test to determine treatment, patients and providers should have the peace of mind to know that their test has been independently verified to ensure it is valid, reliable, safe and

effective. **CLIA oversight of laboratories does not offer such assurances for the performance of tests**, like *BRCA1/2*, which are used to make high-risk medical decisions. Only tests reviewed by the FDA, such as the BRACAnalysis CDx, have been independently verified to ensure their analytical and clinical validity.

- (3) Use of a **companion diagnostic testing for *BRCA1/2* does not and should not preclude any additional diagnostic testing** to determine eligibility for future personalized therapies or to determine hereditary risk, which may use different companion diagnostic tests or multigene panels.
- (4) The FDA label for olaparib states that the drug must be given in combination with use of the approved companion diagnostic test. **Any use of the drug without the approved companion diagnostic could constitute “off label” use and leave patients liable for the cost of the drug**, creating financial stress and distress for the patient. The NCCN itself has issued recommendations to physicians on alleviating distress, including financial stress, among oncology patients in the past and we therefore urge NCCN to reconsider a policy which could result in substantial cost-shifting to patients.

Again, we urge NCCN to strike “or other validated test performed in a CLIA-approved facility” from footnote “g” when discussing selection criteria for olaparib in its 2015 Guidelines for Ovarian Cancer treatment. Opening the door for physicians to use non-approved tests in the ordering of olaparib could jeopardize patient safety and lead to a number of unintended consequences.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'Calaneet H. Balas', with a stylized, cursive script.

Calaneet H. Balas
Chief Executive Officer
Ovarian Cancer National Alliance