ASPiRA LABS
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Submitted by:
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Date of request: October 24, 2017
NCCN Guidelines Panel:

On behalf of Vermillion/ASPiRA Laboratories, I respectfully request the NCCN Clinical Practice Guidelines in Oncology: Ovarian Cancer to review the enclosed data for inclusion of the Multivariate Index Assay test OVA1 in both the Ovarian Cancer TOC Discussion and the Table of Contents Discussion.

Specific Changes:

1. Recommend on page M-5 that you change the wording to "Based on data documenting an increased survival, NCCN Guidelines Panel Members recommend that all patients *with an elevated OVA1 result* should undergo surgery by an experienced gynecologic oncologist"
2. Recommend on page OV-1 that "OVA1 and/or MIA or other tumor markers as clinically indicated" is included to the "Work Up" section as MIA is now recognized as a Level B Recommendation in the ACOG Practice Bulletin #174..
3. Recommend on page OV-1 under the "Primary Treatment" section you add "Establish baseline CA125 as clinically indicated either from OVA1 and/or MIA result or separately."

FDA Clearance: The OVA1 Test is a qualitative serum test that combines the results of five immunoassays into a single numerical score. It is indicated for women who meet the following criteria: over age 18; ovarian adnexal mass present for which surgery is planned, and not yet referred to an oncologist. The OVA1 Test is an aid to further assess the likelihood that malignancy is present when the physician's independent clinical and radiological evaluation does not indicate malignancy. The test is not intended as a screening or stand-alone diagnostic assay.

Rationale: In light of the recent inclusion of Multivariate Index Assay (MIA) to the latest ACOG Practice Bulletin on the Evaluation and Management of Adnexal Masses (#174 published November 2016), we feel it is important for practitioners to know that the OVA1 FDA Cleared test is the only test proven to determine risk of malignancy across all histologic subtypes and menopausal statuses prior to operating, thus avoiding any missed malignancies being operated on by a generalist and patients suffering worse prognoses. Furthermore, with just under 1000 board certified Gynecological Oncologists in this country, a refer all recommendation may lead to delayed diagnosis and treatment. The CA125 level is now reported out on our results with every OVA1 score, giving ordering providers both an effective risk assessment score and an early baseline CA125 level for those ultimately diagnosed with ovarian cancer.

The following articles are submitted in support of these proposed changes. We would like to acknowledge the tireless work of the NCCN Panel Members who are trying to improve the outcomes for women with ovarian cancer just as we are.

1. The American College of Obstetricians and Gynecologists Praqctice Bulletin #174, November 2016 (replaces PB #83). "Evaluation and Management of Adnexal Masses".
2. Urban, R, et.al. "Evaluation of a Validated Biomarker Test in Combination With a Symptom Index to Predict Ovarian Malignancy". *Int J Gynecol Cancer.* 2017 Feb;27(2):233-238.
3. Eskander et a. *Current Medical Research and Opinion,* 2016 32:6, 1161-1165 "The clinical utility of an elevated-risk multivariate index assay score in ovarian cancer patients"

Sincerely,

MD.

Marra S. Francis, MD, FACOG, Chief Medical Officer Vermillion, Inc.