# ROMA or OVA1 Improves Identification and Treatment of Women With Ovarian Cancer

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Although it is well recognized that surgical staging improves survival in women with ovarian cancer, survival outcomes in these women remain low. According to 2007 Surveillance, Epidemiology, and End Results (SEER) data, 10-year survival rates for a woman with stage III and one with stage IV ovarian cancer are just over 22% and 10%, respectively [Ries L et al. *National Cancer Institute: SEER Program* 2007]. For unstaged ovarian cancer, the survival rate is just over 20%.

Evidence shows that survival rates are significantly higher in women at high risk of ovarian cancer who are surgically staged by a gynecologic surgeon at a high-volume hospital [Paulsen T et al. *Int J Gynecol Cancer* 2006]. However, treatment remains suboptimal in part because high-risk patients are often not identified and triaged to the appropriate surgeon and institution.

Ways to improve identification of women with a pelvic mass at high risk of ovarian cancer were discussed during the John and Marney Mathers Lecture titled "Pelvic Mass Risk Assessment: Could It Be Cancer?" at the 2014 American Congress of Obstetrics and Gynecology (ACOG) annual meeting. David Scott Miller, MD, Division of Gynecologic Oncology, University of Texas Southwestern Medical Center, Dallas, Texas, USA, and Richard Moore, MD, Program in Women's Oncology, Department of Obstetrics and Gynecology, Women and Infants' Hospital of Rhode Island, Alpert Medical School, Brown University, Providence, Rhode Island, USA, presented information on 2 algorithms currently approved by the Food and Drug Administration to improve identification of high-risk women with the goal of triaging these women to optimal care.

According to Dr. Moore, both ROMA (Risk of Ovarian Malignancy Algorithm) and OVA1 are very good at identifying ovarian masses at high risk of ovarian cancer, particularly when the algorithm is combined with clinical assessment. He said it is up to each physician to determine which test to use, but he emphasized the need to use only one algorithm and not both.

Both Dr. Moore and Dr. Miller highlighted some differences between the two tests, however, that were useful in understanding their particular potential strengths and limitations. The session opened with a brief discussion of the ACOG-SGO (–Society of Gynecologic Oncology) guidelines on the clinical assessment of pelvic masses for the evaluation and triage of adnexal masses (Table 1), which are used in conjunction with each algorithm for optimal predictive value [Committee Opinion No. 477 ACOG. *Obstet Gynecol* 2011].

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Table 1. Clinical Assessment Using ACOG-SGO Guidelines: Referral Criteria for Women With Adnexal Masses to Gynecologic Oncologists

| Premenopausal | Postmenopausal |
|---|---|
| CA125: "very elevated" | CA1235: "elevated" |
| Ascites | Ascites |
| Evidence of abdominal/distant metastases | Nodular/fixed pelvic mass |
| – | Evidence of abdominal/distant metastases |

ACOG-SGO=American Congress of Obstetrics and Gynecology–Society of Gynecologic Oncology.

## BENEFITS OF OVA1

One main benefit of OVA1 cited by both Dr. Miller and Dr. Moore is its greater sensitivity, compared with ROMA, for identifying ovarian cancer in women initially assessed with benign disease.

Dr. Miller highlighted data on OVA1 that, in his opinion, make this algorithm superior to ROMA, particularly for patients with early stage disease and nonepithelial ovarian cancers. He cited the only head-to-head study of 70 premenopausal women and 76 postmenopausal women that looked at the predictive value of OVA1 compared with ROMA for the detection of ovarian cancer in women with a pelvic mass [Grenache DG et al. *J Clin Oncol* 2013]. The authors of the study found a similar performance between the two methods, but found that OVA1 had a greater sensitivity for identifying ovarian cancer in women initially assessed with benign disease, whereas ROMA had a higher specificity for identifying women who did not have ovarian cancer.

Overall, when OVA1 is combined with clinical assessment, the evidence shows that OVA1 has an average sensitivity of 96% for a broad range of ovarian malignancies [Moore RG et al. *Obstet Gynecol* 2011; Ueland FR et al. *Obstet Gynecol* 2011]. Providing additional confidence of the predictive ability of OVA1 is the evidence showing that OVA1 also has a high negative predictive value (NPV; 95% to 98%) [Ueland FR et al. *Obstet Gynecol* 2011], which is the probability that a patient with a negative test result really does not have ovarian cancer.

Dr. Miller emphasized that OVA1 is well validated, having been used in more than 1000 patients and 250 malignancies. He also said the test is easy to use and interpret, making triage more efficient and allowing low-risk patients to remain with the general gynecologist.

## BENEFITS OF ROMA

Dr. Moore emphasized that the main benefit of ROMA over OVA1 is its better ability to detect invasive ovarian cancer as shown by its greater specificity than OVA1. He emphasized that detecting invasive cancer is what is important, and not detection of low malignant potential tumors that would not need a second surgery for debulking or determining chemotherapy. Therefore, fewer patients with benign masses will be referred to tertiary centers by using ROMA.

He cited data from two validation studies that showed the high specificity of ROMA. The first study showed that ROMA was able to correctly identify 94% of all invasive cancers (95% in postmenopausal women and 89% in premenopausal women) [Moore RG et al. *Gynecol Oncol* 2009], and the second study showed that ROMA correctly identified 93.8% of all invasive cancers (92.3% in postmenopausal women and 100% in premenopausal women) [Moore RG et al. *Obstet Gynecol* 2011].

To show the greater specificity of ROMA compared with OVA1, he used data from the FDA submission of each method (Table 2). These data also show the high sensitivity and NPV of ROMA, similar to that of OVA1.

Table 2. Greater Specificity of ROMA Compared With OVA1 in Detecting Cancers (Ovarian and Nonovarian)

| Statistical Parameter | ROMA | OVA1 |
|---|---|---|
| No. of women | 468 | 269 |
| Sensitivity | 89.7% | 87.5% |
| Specificity | 49.1% | 50.8% |
| Negative predictive value | 95.4% | 91.7% |
| Positive predictive value | 28.7% | 39.4% |
| Prevalence | 19% | 26.8% |

Results based on a Stand-Alone Test, where pre- and postmenopausal patients were evaluated by non–gynecologic oncologists.

Another benefit of ROMA over OVA1, he emphasized, is that ROMA has been validated by more than 12 independent studies. This has been done, he said, because ROMA is available to anyone for use and, unlike OVAI, is not proprietary. Other benefits are shown in Table 3.

Table 3. Comparison of ROMA and OVA1

| Parameter | ROMA | OVA1 |
|---|---|---|
| Sensitivity for EOC | 94% | 95% |
| Specificity for EOC | 75% | ≈50% |
| Biomarker levels resulted | Yes (CA125 and HE4) | No |
| Cost | $120 | $600 |
| Lab | Any lab | Only 1 lab |
| Algorithm | Published | Black box |
| Independently validated | Yes (>12) | No |

EOC=epithelial ovarian cancer.

Both OAV1 and ROMA improve detection of women at high risk of ovarian cancer, particularly when combined with clinical assessment, and permit better triaging of patients to the appropriate surgeon and hospital for optimal care [Moore RG et al. *Obstet Gynecol* 2011; Ueland FR et al. *Obstet Gynecol* 2011; Miller et al. *Obstet Gynecol* 2011]. This is represented by the high sensitivity and the negative predictive value of both algorithms. The higher specificity of ROMA, according to Dr. Moore, indicates its greater value in correctly identifying women at high risk of ovarian cancer and better ensures that women with benign disease will not be triaged to a tertiary care center for care by an oncologic surgeon.