



Overview

OVA1® is a multi-marker blood test that can aid physicians in the pre-operative clinical assessment of an ovarian adnexal mass. In a prospective, multi-center study, dual assessment using OVA1 in conjunction with clinical assessment was found to detect more cancers than clinical assessment alone. Moreover, OVA1 in conjunction with clinical assessment detected 79% of stage I ovarian cancer and all stage II/III ovarian cancer. These results indicate that OVA1, when used in conjunction with clinical assessment, can improve the detection of malignant ovarian tumors.

Intended Use

OVA1 is a qualitative serum test that combines the results of five immunoassays into a single numerical result. 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. OVA1 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.

PRECAUTION: OVA1 should not be used without an independent clinical/radiological evaluation and is **not** intended to be a screening test or to determine whether a patient should proceed to surgery. Incorrect use of OVA1 carries the risk of unnecessary testing, surgery, and/or delayed diagnosis.

Summary and Explanation of the Test

Ovarian tumors are being detected with increasing frequency in women of all ages. There are numerous recent publications clarifying the importance of a gynecologic oncologist in the care of subjects with ovarian cancer. The National Comprehensive Cancer Network (NCCN)¹ and the Society of Gynecologic Oncologists (SGO)² plus other studies have demonstrated the value of referring subjects with ovarian cancer to gynecologic oncologists for their surgery^{3,4}.

OVA1 should be used in conjunction with imaging studies and other clinical assessment in a woman for whom surgical intervention is planned. OVA1 can assist the decision-making process of whether to refer the subject to a gynecologic oncologist, when the referring physician's presurgical assessment does not indicate malignancy.

Clinical Study Results

OVA1 was evaluated in a prospective, double-blind clinical study. The clinical study subject enrollment centers were representative of institutions where ovarian tumor subjects potentially undergo a gynecologic examination. The specimens were collected at 27 demographically mixed sites that included large and small medical centers (universities/community hospitals), clinics that specialize in women's health, small gynecology/obstetrics groups, gynecology/oncology practices, and HMO groups).

1. NCCN Ovarian Cancer Practice Guidelines. The National Comprehensive Cancer Network. Oncology (Williston Park), 10: 293-310, 1996.

2. Hoskins, W. et al, Society of Surgical Oncology practice guidelines. Oncology (Williston Park), 11: 896-900, 903-4, 1997.

3. Earle, C. C. et al, Effect of surgeon specialty on processes of care and outcomes for ovarian cancer patients. JNCI, 98:172-80, 2006

4. Giede, K. C., et al Who should operate on patients with ovarian cancer? An evidence-based review. Gynecol Oncol, 99: 447-61, 2005.

Demographic Characteristics

The OVA1 analysis was performed on 516 individual serum specimens collected prospectively from women who met the study inclusion criteria and proceeded to surgery for an ovarian mass. Within the study there were 235 (45.5%) pre-menopausal women and 281 (54.5%) post-menopausal women, each of whom were self identified. Of the 235 pre-menopausal women, 144 (61.2%) were evaluated by a non-GO (non gynecological oncologist) and 91 (38.7%) were evaluated by a GO (gynecological oncologist). Of the 281 post-menopausal women, 125 (49.8%) were evaluated by a non-GO and 156 (51.2%) were evaluated by a GO. The following table provides information pertaining to the pathology diagnosis.

Table 1: Demographic characteristics and pathology results or physician assessment results for all evaluable subjects.

	All Evaluable Subjects w/ Pre-surgical Assessment (N= 516)	Non-GO Physicians (N= 269)	GO Physicians (N= 247)
AGE, YEARS			
N	516	269	247
Mean (SD)	52.0 (13.9)	49.7 (13.6)	54.6 (13.8)
Range (min, max)	18 to 92	19 to 90	18 to 92
Premenopausal, n (%)	235 (45.5%)	144 (53.5%)	91 (36.8%)
Postmenopausal, n (%)	281 (54.5%)	125 (46.5%)	156 (63.2%)
PATHOLOGY DIAGNOSIS, n (%)			
Benign ovarian conditions	355 (68.8%)	197 (73.2%)	158 (64.0%)
Epithelial ovarian cancer (EOC)	96 (18.6%)	45 (16.7%)	51 (20.6%)
Other primary ovarian malignancies (non EOC)	9 (1.7%)	5 (1.9%)	4 (1.6%)
Ovarian tumors with low malignant potential (Borderline)	28 (5.4%)	12 (4.5%)	16 (6.5%)
Non-ovarian malignancies with involvement of the ovaries	18 (3.5%)	5 (1.9%)	13 (5.3%)
Non-ovarian malignancies with no involvement of ovaries	10 (1.9%)	5 (1.9%)	5 (2.0%)

Patients are assigned a unitless result between 0.0 and 10.0 by the OvaCalc software; the result is called the OVA1 score. This result is given in the OVA1 test report written below:

<i>Pre-menopausal:</i>	<i>Low probability of malignancy</i>	<i>OVA1 < 5.0</i>
	<i>High probability of malignancy</i>	<i>OVA1 ≥ 5.0</i>
<i>Post-menopausal:</i>	<i>Low probability of malignancy</i>	<i>OVA1 < 4.4</i>
	<i>High probability of malignancy</i>	<i>OVA1 ≥ 4.4</i>

Single & Dual Assessment

The information provided by OVA1 should be used by the physician as an adjunctive test to complement, not replace, other diagnostic and clinical procedures. To demonstrate that OVA1 provides additional information when used in combination with the physician's pre-surgical assessment, the ability of OVA1 to contribute to the physician's pre-surgical assessment was analyzed. The OVA1 analysis is based upon two measurements, either a single assessment comprising pre-surgical clinical impression, or, a dual assessment (OVA1 and the clinical assessment).

The following table shows results for all subjects evaluated by a non-GO with "positive" results for likely malignancy either based on a positive presurgical assessment alone (single assessment), or based on a positive result from the presurgical assessment or from the OVA1 result or from both (dual assessment).

Table 2. All subjects evaluated by non-GO physicians.

Performance	Single assessment (pre-surgical assessment)	Dual assessment (pre-surgical assessment & OVA1 result used)
Sensitivity 95% CI	72.2% (52/72) 61.0% to 81.2%	91.7% (66/72) 83.0% to 96.1%
Specificity 95% CI	82.7% (163/197) 76.9% to 87.4%	41.6% (82/197) 35.0% to 48.6%
Positive Predictive value (PPV) 95% CI	60.4% (52/86) 49.9% to 70.1%	36.5% (66/181) 29.8% to 43.7%
Negative Predictive Value (NPV) 95% CI	89.1% (163/183) 83.7% to 92.8%	93.2% (82/88) 85.9% to 96.8%
Prevalence	26.8% (72/269)	

With dual assessment, sensitivity for malignancy increased from 72% (52/72) to 92% (66/72). That is, approximately two-thirds of the malignancies missed by pre-surgical assessment alone were called positive if a dual assessment including clinical assessment and OVA1 was used. Specificity for malignant diagnoses decreased from 83% to 42% with dual assessment. NPV of the dual assessment increased from 89% to 93%, supporting improved performance by dual assessment and strengthens the predictions that cancer is absent. Overall, non-GO and GO dual assessment using OVA1 detected 82.5% (33/40) cases missed by clinical assessment alone.

Stage Distribution

A summary of OVA1 results by cancer stage for evaluable subjects with a primary ovarian malignancy (EOC and non-EOC combined) are detailed in the table below. OVA1 correctly identified 100% of the malignant adnexal masses in stages two and three and 79% in stage one.

Table 3: OVA1 Results by Cancer Stage^a for primary ovarian malignancies in all evaluable subjects with a pre-surgical clinical assessment from non-GO.

	Stage I	Stage II	Stage III
No. of Subjects	14	11	25
OVA1 Mean (SD)	6.89 (2.313)	8.21 (1.600)	8.36 (1.289)
Median	6.55	8.60	8.70
Range (min, max)	3.6 to 10.0	5.1 to 10.0	5.5 to 10.0
OVA1 Positive	11	11	25
OVA1 Negative	3	0	0
OVA1 Sensitivity	78.6 %	100%	100%

^a No Stage IV Patients were evaluated by non-GO

Summary

OVA1 provides new, objective information to help physicians refer women to the most appropriate surgeon to operate on her ovarian mass -- potentially helping to promote better treatment outcomes. OVA1 in conjunction with clinical assessment has been shown to identify more malignant ovarian tumors than clinical assessment alone.

OVA1 detected more cancers (14/20 from non-GO's and 33/40 overall) than standard preoperative assessments (clinical and radiological evaluations). Additionally, sensitivity increased from 60% (preoperative assessment) to 89% (preoperative assessment plus OVA1) in premenopausal women and from 81% to 98% in postmenopausal women. For women with an ovarian mass for whom surgery is planned, OVA1 assists in the identification of likely malignancy for potential referral to gynecologic oncologists.

This document is intended only as a summary of the OVA1 Instructions For Use for non Gynecologic Oncologists. For the full Instructions For Use or more detailed information, please send an email to info@vermillion.com with your request for more information.