

# OvPlex™

## Ovarian Cancer Test



### OVERVIEW

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Despite advances in molecular biology, surgical oncology, and chemotherapy, the prognosis for ovarian cancer remains poor. The excellent survival rates for stage I disease provide the rationale for efforts to screen for early-stage ovarian cancer (Rosenthal 1998). Earlier detection remains the most promising approach to improve long-term survival of patients with ovarian cancer (Zhang 2004).

**OvPlex™** is a multimarker blood test for the diagnosis of ovarian cancer that displays better diagnostic efficiency than the CA125 blood test. It has demonstrated efficacy for the detection of early stage (Stage I and II) disease.

OvPlex™ measures 5 serum markers, one of which is CA125. The four additional markers, that deliver improved efficiency, are acute phase response markers to cancer. The five test results are processed using a multivariate algorithm to generate a single OvPlex™ value (i.e. the likelihood a woman has ovarian cancer).

Based upon the analysis of Receiver Operator Characteristic (ROC) Curves, OvPlex™ significantly out performs the CA125 blood test, for both early and late stage disease. **For the detection of ovarian cancer**, OvPlex™ delivers 91.3% specificity, 94.1% sensitivity and an overall diagnostic efficiency of 92.7%. (Based on early stage disease only, OvPlex™ delivers 91.3% specificity, 91.9% sensitivity and an overall diagnostic efficiency of 91.6%.)

#### **Specimen Collection**

*Once the medical practitioner has given the patient their request form, the patient should contact ARL Pathology on 1300 554 480 to obtain an OvPlex™ Collection Kit or order online at [www.arlpath.com.au](http://www.arlpath.com.au)*

*Following receipt of the kit:*

- 1. Melbourne patients may have blood collected at any of the ARL Pathology Collection Centres (see "Collection Centres" or [www.arlpath.com.au](http://www.arlpath.com.au))*
- 2. Interstate patients may have their blood specimen taken at their nearest pathology collection centre and must then be sent to ARL Pathology for analysis. The collecting pathology lab may charge a fee for this service.*

#### **Turnaround Time**

Turnaround time is the number of days it takes from ARL Pathology receiving the specimen/s and sending the result to the practitioner. Test results are usually available within 10-20 working days.

#### **Test Results**

Test results can be downloaded electronically by the medical practitioners if requested. They can also be sent to the practitioner by mail or fax. Medical practitioners can contact ARL Pathology on 1300 554 480 to set up your requirements.

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### What to do next?

Steps to follow:

1. Order an OvPlex™ ovarian cancer test kit from ARL Pathology.
2. Take the kit including the enclosed request form to your doctor. Please note: If you are taking any anti-inflammatory medications please discuss with your doctor as you will be required to stop taking this medication(s) for 5 days prior to specimen collection\*. Fasting is not required for these tests.
3. Collection of blood samples.
  - a) You are able to attend an [ARL Pathology \(or associated\) collection centre](#) Monday to Friday.
  - b) If there is no ARL Pathology collection centre in your area you may have the samples collected by another pathology company collection centre. Please note collections in this way can only occur on a Monday, Tuesday or Wednesday.

### What is the cost?

\$200 (no Medicare or private health fund rebate is currently available).

A collection fee of \$30 will be charged if you attend another pathology provider other than ARL Pathology.

NB: Pathology providers other than ARL Pathology may in some cases charge an additional fee.

Testing cannot proceed without full payment of the kit.

### How and when will I receive my results?

Results will be forwarded to your doctor within 10-20 working days.

A kit can be ordered online from [www.arlpath.com.au](http://www.arlpath.com.au)

\* Classification of anti-inflammatory medication should be discussed with your doctor. Furthermore, any change or modifications in medications and their schedule should also be discussed fully with your doctor prior to this test being performed.

### Test Kit

Once the practitioner has given the patient their request form, the patient can order their test kit online, [www.arlpath.com.au](http://www.arlpath.com.au) or by calling ARL Pathology customer service on **1300 55 44 80** between the hours of 8:30 and 5:30 (EST). The test kit contains full instructions.

### Specimen Requirements

Two small blood samples are collected. *Fasting is not required beforehand.*

### Technical Support

The OvPlex™ test will be accompanied by Interpretive Comments to assist practitioners in their clinical understanding and patient management for each result.

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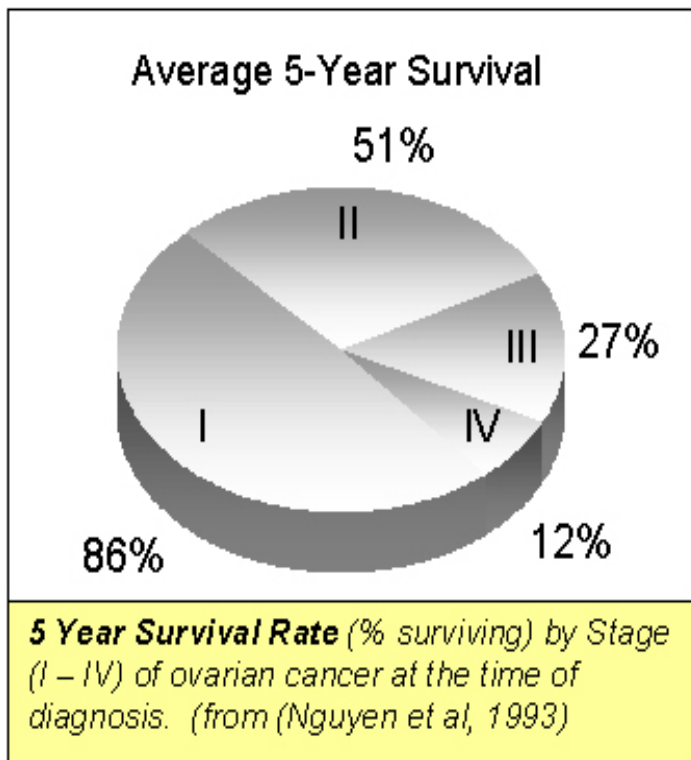
## Ovarian Cancer Test

**Ovarian cancer** continues to be the leading cause of death among women with gynaecological malignancies. It is the fourth most common cause of cancer-related deaths in women in Australia. Each year, ovarian cancer affects ~1500 Australian women and results in 800 deaths.

Due to the absence of overt symptoms, the majority of cases (75%) are diagnosed at an advanced stage (Stage III/IV) (Rosenthal & Jacobs, 1998). As conventional treatments have a poor success rate for disseminated disease, average 5-year survival rate is 12 - 27% (Nguyen *et al*, 1993). If, however, ovarian cancer is detected early 5-year survival is dramatically improved (86% for Stage I).

Improved screening to permit early diagnosis of ovarian cancer will greatly improve the outlook for ovarian cancer patients using conventional treatments.

The measurement of serum concentrations of CA125, a high-molecular-weight mucin (MUC 16), currently used for confirmation of ovarian cancer diagnosis and monitoring treatment response and disease recurrence, however, only delivers an overall sensitivity of 50% to 60% for stage I disease (Jacobs & Bast, 1989).



Recent trials of multimarker blood tests have reported improved sensitivity and specificity for detecting early stage ovarian cancer. (Visintin *et al* 2008, Zhang *et al*, 2004)

### Symptoms Associated with Ovarian Cancer

The most common symptoms are:

- bloating;
- pelvic or abdominal pain;
- trouble eating or feeling full quickly; and
- urinary symptoms, such as urgency and frequency.

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Symptoms such as the ones listed above are, of course, relatively common and occur with any number of ailments. In fact, they are more likely to be due to causes other than ovarian cancer. But when their occurrence is unusual, when they are present almost daily, and when they last for more than a few weeks, they should prompt a woman to see a doctor, preferably a gynaecologist, the cancer groups recommend.

Other symptoms of ovarian cancer can include:

- fatigue;
- upset stomach;
- back pain;
- pain during intercourse;
- constipation; and
- menstrual changes.

### OvPlex™ Assay Performance

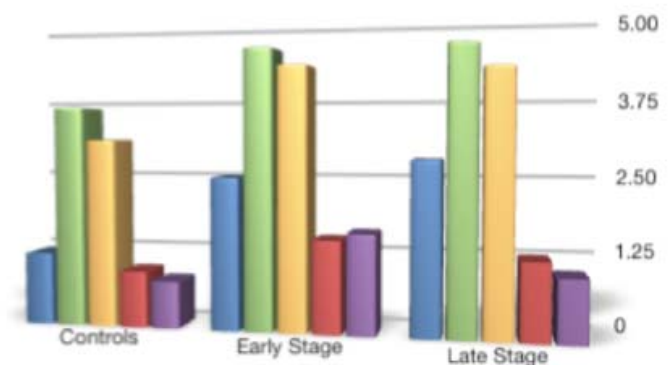
In a study comprising more than 350 control and disease samples, ROC curve analysis demonstrates that the OvPlex™ Biomarker Panel has greater diagnostic performance than CA125.

The 5 biomarker measurements are submitted to a modelling program that generates the OvPlex™ Index - the probability the subject has ovarian cancer.

Improvement in diagnostic efficiency is even more evident when considering the diagnosis of early stage ovarian cancer. OvPlex™ displays a diagnostic efficiency of 91.6 %.

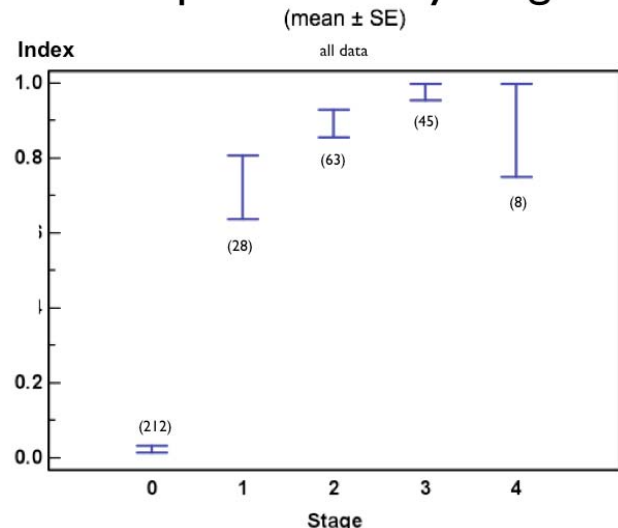
The use of OvPlex™ is associated with a 2-3 fold reduction in the number of false positive diagnoses when compared to CA125.

The OvPlex™ test reports a value between 0 and 1. OvPlex™ values of greater than 0.30 are indicative of a higher than normal risk of ovarian cancer and it is recommended that the patient be referred to a gynaecologist for further assessment.



Plasma concentrations (log values) of the individual 5 biomarkers in control, early stage and late stage ovarian cancer

### Ovplex Index by Stage



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OvPlex™ values below 0.30 and CA125 < 35 U/ml is indicative of a low risk of ovarian cancer.

For early stage disease (i.e. Stage I and II) OvPlex™ displays a sensitivity of 91.9%.

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### Reference

Jacobs I, Bast RC (1989) The CA125 tumor-associated antigen - a review of the literature. *Hum Reprod* **4**: 1-12

Nguyen HN, Averette HE, Hoskins W, Penalver M, Sevin BU, Steren A (1993) National survey of ovarian carcinoma. Part V. The impact of physician's specialty on patients' survival. *Cancer* **72**: 3663-70

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Visintin I, Feng Z, Longton G, Ward D.C., Alvero A.B., Lai Y, Tenthorey J., Leiser A., Flores-Saaib R., Yu H. , Azori M., Rutherford T., Schwartz P.E., and Mor G. (2008) Diagnostic Markers for Early Detection of Ovarian Cancer *Clin Cancer Res* **14**:1065-1072.

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