



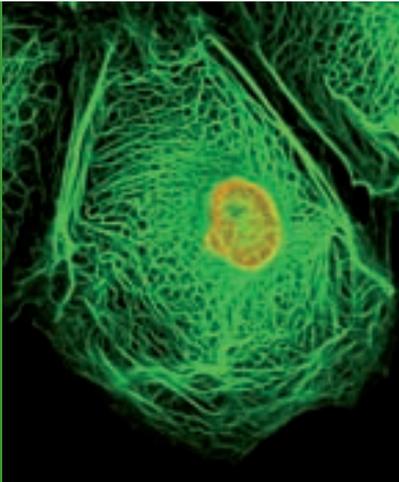
# ARCHITECT HE4\*

Human Epididymal Protein 4

## Role of HE4 for management of patients presenting with pelvic mass

Ovarian cancer is the most common form of reproductive cancer in women worldwide and the leading cause of death from gynaecological cancer. If caught during the early stages, the patient has an excellent prognosis. However, in 70% of cases, patients are diagnosed during the advanced stages of the disease when the survival rate is very poor. Only 10–30% of these patients survive beyond one year. Currently, less than half of ovarian cancer patients have their diagnostic surgery with a gynaecologic oncologist trained in the management of ovarian cancer causes further reduction in survival rates.

The multiple marker assay combining CA 125 and HE4 can be used to triage patients to the appropriate specialist.



## Human Epididymal Protein 4 (HE4)

HE4 is a useful biomarker for the detection of ovarian cancer with only a minimal expression in normal ovarian tissue. In addition to expression on a cellular level, high levels of secreted HE4 were detected in the serum of ovarian cancer patients. HE4 achieved 96% specificity and 80% sensitivity comparing healthy subjects and cancer patients.

(Source: R. G. Moore et al., *Gynecol. Oncol* 2008; 108: 402 – 408)

## ARCHITECT HE4\*

A fully automated test used to estimate the risk of ovarian cancer in premenopausal and postmenopausal women presenting with pelvic mass when used in conjunction with the ARCHITECT CA 125 II assay. The assay has a dynamic range that extends to 1500 pmol/L. Time to first result for ARCHITECT HE4\* is 28 minutes with the ability to perform 200 samples per hour.

CA 125 + HE4 = Risk Stratification

\* in development

## Estimates of Sensitivity

Average from Leave One-Out Analysis Marker Combination	Benign vs. Ovarian Cancer: Sensitivity at		
	90% Specificity	95% Specificity	98% Specificity
CA 125	61.2%	43.3%	23.9%
HE4	77.6%	72.9%	64.2%
CA 125 + HE4	<b>80.7%</b>	<b>76.4%</b>	<b>71.6%</b>
CA 125 + HE4 + SMRP <sup>†</sup>	80.6%	74.7%	71.7%
CA 125 + HE4 + CA72-4	82.1%	78.8%	71.5%

<sup>†</sup> SMRP: soluble mesothelin-related peptide

R. G. Moore et al., *Gynecologic Oncology* 2008; 402 – 408

- As a single marker, HE4 was more sensitive than CA 125
- The combination of HE4 and CA 125 was more sensitive than either marker alone
- Additionally, for Stage 1 disease, HE4 alone was the most sensitive marker

## Conclusions from Publications

“In comparison with normal surface epithelium, which does not express HE4, we found that cortical inclusion cysts lined by metaplastic Mullerian epithelium abundantly express the protein.”

“Its expression in tumors was restricted to certain histologic subtype: 93 % of serous and 100 % of endometrioid EOCs expressed HE4.”

*B. Drapkin et al., Cancer Res 2005; 65: (6)*

“Of all the tumor markers in the current study, HE4 had the highest sensitivity as a single marker, findings consistent with those reported by Hellström et al. The combination of the two serum biomarkers CA 125 and HE4 increased the sensitivity when compared to either marker alone.”

*R. G. Moore et al., Gynecol Oncol 2008; 108: 402 – 408*

“HE4 demonstrated the highest sensitivity in identifying both early (stage I/II) and late (stage III) ovarian cancer. Sensitivity ranged from 62.4–82.7% for early stage and 74.6–92.5% in late stage, depending on the cutoff value that was used.”

*L. J. Havrilesky et al., Gynecol Oncol 2008; 110: 374 – 382*

“An algorithm utilizing HE4 and CA 125 successfully classified patients into high and low risk groups with 93.8% of EOC correctly classified as high risk. This model can be used to effectively triage patients to centers of excellence.”

*R. G. Moore et al., Gynecol Oncol 2008, in press*