DiaSino® HE4 ELISA

Early biomarker for monitoring and management of ovarian cancer

diasino®

HE4

Early marker with increased sensitivity for ovarian cancer

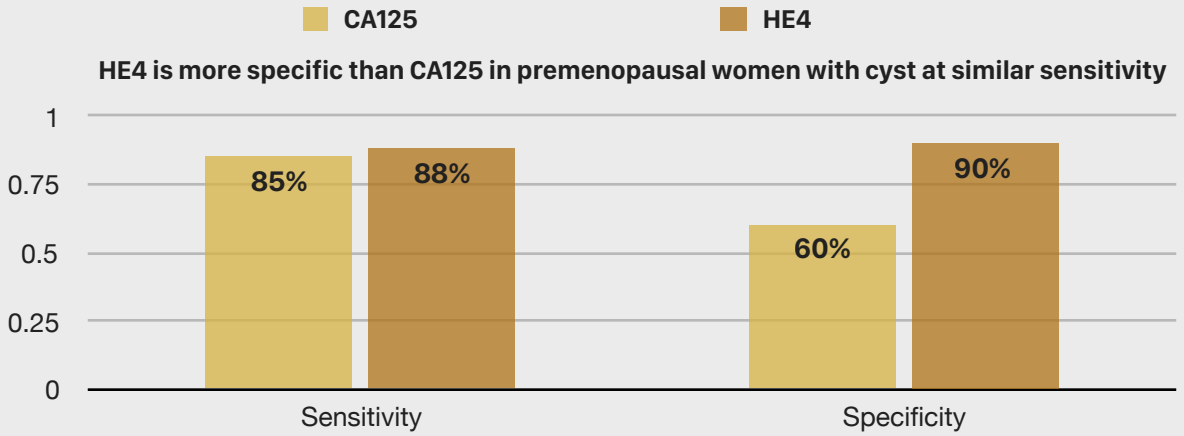
- As a single tumor marker, HE4 had the highest sensitivity (at a specificity of 75%) for detecting ovarian cancer, especially in stage I diseases, the early non-symptomatic stage.[5,6]
- Additionally, several publications have reported that HE4 yielded a up to 17% higher sensitivity in early-stage endometrial cancer compared to CA125.[7,8]
- Elevated serum HE4 with normal CA125 would suggest the presence of either ovarian or other type of cancer, for example endometrial cancer.[8]

Good discrimination between benign ovarian masses and cysts and ovary cancer

- Combination of HE4 and CA125 can help in determining whether a pelvic mass is benign or malignant in pre- and post- menopausal women (see ROMA fact sheet).
- The dual marker combination CA125 and HE4 is a more accurate predictor of malignancy than either alone. Huhtinen et al. reported a 78.6% sensitivity at 95% specificity in ovarian carcinoma vs. endometriotic cysts.[8]

HE4 supports CA125 to better monitor ovarian cancer

- HE4 can be used to monitor the disease status in ovarian cancer patients. HE4 levels correlate with clinical response to therapy or recurrence status in women with diagnosis of ovarian carcinoma as determined by CT imaging.[9] HE4 could be an important early indicator for disease recurrence.[10-12]
- In most of ovarian cancer patients both markers are expressed in significant amounts, but there are patients who are positive for only one of the biomarkers HE4 or CA125. The combined use of CA125 and HE4 could facilitate the detection of recurrent disease by reducing the number of biomarker negative patients higher diagnostic accuracy.
- Cysts are a common occurrence, especially in premenopausal women, and the majority of cysts are benign.Up to 10% of women will have some form of surgery for ovarian mass.[13] HE4 is more specific than CA125 in premenopausal women with cyst at similar sensitivity.[14]



DiaSino® HE4 test characteristics

Testing time	80 minutes
Test principle	One-step sandwich principle
Calibrators	0, 50, 150, 300, 600, 1200 pmol/L
Sample material	Serum, Li–heparin, K2–EDTA and K3–EDTA plasma
Sample volume	25 µL
Detection limit	15 pmol/L
Measuring range	15-1200 pmol/L
Traceability	Fujirebio HE4 ELISA

Expected values: ≤ 140 pmol/L

A study in one clinical center in China with the DiaSino HE4 assay on sera from 277 apparently healthy women yielded the following results:

HE4 (pmol/L)

Age (years)	N	Median	95th percentile
<40	98	45.6	62.8
40-49	51	44.2	70.7
50-59	50	56.7	78.4
60-69	50	60.3	88.6
≥70	28	65.1	102.4

The distribution of HE4 assay values determined one clinical center in China with the DiaSino HE4 assay in 476 female specimens is summarized in the table below:

HE4 values (pmol/L)		0.0-70	70.1-140	140.1-500	500.1-1500	>1500
		N (Percentage distribution)				
Apparently healthy						
Premenopausal	48	41 (85.4%)	6 (12.5%)	1 (2.1%)	0 (0.0%)	0 (0.0%)
Postmenopausal	57	34 (59.6%)	21 (36.8%)	2 (3.5%)	0 (0.0%)	0 (0.0%)
Benign conditions						
Premenopausal	97	87 (89.7%)	9 (9.3%)	1 (1.0%)	0 (0.0%)	0 (0.0%)
Postmenopausal	52	32 (61.5%)	16 (30.8%)	4 (7.7%)	0 (0.0%)	0 (0.0%)
Pregnancy	25	25 (100%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-gynecological disease	19	9 (47.4%)	4 (21.1%)	3 (15.8%)	0 (0.0%)	0 (0.0%)
CHF[a]	14	6 (42.9%)	6 (42.9%)	2 (14.3%)	0 (0.0%)	0 (0.0%)
Cancer						
OvCa[b], premenopausal	20	6 (30.0%)	4 (20.0%)	7 (35.0%)	2 (10.0%)	1 (5.0%)
OvCa, postmenopausal	51	5 (9.8%)	9 (17.6%)	18 (35.3%)	16 (31.4%)	3 (5.9%)
Endometrial	26	9 (34.6%)	11 (42.3%)	4 (15.4%)	1 (3.8%)	1 (3.8%)
Breast	24	11 (45.8%)	10 (41.7%)	2 (8.3%)	1 (4.2%)	0 (0.0%)
Gastrointestinal	23	10 (43.5%)	11 (47.8%)	2 (8.7%)	0 (0.0%)	0 (0.0%)
Lung	13	3 (23.1%)	4 (30.8%)	6 (46.2%)	0 (0.0%)	0 (0.0%)
Bladder	7	2 (28.6%)	2 (28.6%)	2 (28.6%)	1 (14.3%)	0 (0.0%)

[a] CHF = Congestive heart failure

[b] Ovarian cancer

In this study 98% of the apparently healthy women had a HE4 assay value at or below 140 pmol/L. It is recommended that each laboratory establishes its own reference value for the population of interest.

Monitoring of disease status in patients diagnosed with ovarian cancer

The effectiveness of the DiaSino HE4 assay as an aid in monitoring of disease status in ovarian cancer patients was deter mined by assessing changes in HE4 levels in serial serum samples from 100 patients compared to changes in disease status. This follow-up study contained a total of 334 samples with ≥ 3 samples per patient. A positive change in HE4 was defined as an increase in the value that was at least 20% greater than the previous value of the test. This level of change takes into account the variability of the assay and the biological variability.

58.7% (27 of 46) of the patient samples with a positive change correlated with the disease progression while 80.6% (232 of 288) of the patient serial samples with no significant change in HE4 value correlated with no progression.
The total concordance was 77.5% (259 of 334). The following table presents the data in a 2 x 2 format.

Changes in disease state per sequential pair

Increase in HE4 concentration	Progression	No progression	Total
≥ 20%	27	56	83
< 20%	19	232	251
Total	46	288	334

Method comparison

DiaSino HE4 ELISA characteristics to compare with other commercialized players, take Fujirebio/CanAg HE4 as reference

	DiaSino HE4 ELISA	Fujirebio/CanAg HE4 ELISA	Roche Elecsys HE4 ECLIA	Abbott Architect HE4 CMIA
• Manufacturer				
• Assay principle	One-step sandwich	Two-step sandwich	One-step sandwich	One-step sandwich
• Incubation time	80 minutes	180 min	10 min	29 min
• Incubation temp	37℃	RT	37℃	37℃
• Calibrators type	Ready to use	Lyophilized	\	\
• Sample volume	25 µL	25 µL	10 µL	100 µL
• Sample material	Serum/Plasma	Serum	Serum/Plasma	Serum/Plasma
• Limit of detection	15 pmol/L	15 pmol/L	15 pmol/L	20 pmol/L
• Measuring range	15-1200 pmol/L	15-900 pmol/L	15-1500 pmol/L	20-1500 pmol/L
• Total Precision	<10%	15%	< 5%	< 10%
• Traceability	Fujirebio HE4 ELISA	Internal standard	Fujirebio HE4 ELISA	Fujirebio HE4 ELISA
• Hook	< 300, 000 pmol/L	<300,000 pmol/L	< 40,000 pmo/L	<94,000 pmol/L

Order information

Catalog No.	Product	Packaging
DS177731	HE4 ELISA	96 tests
DS177732	CA125 ELISA	96 tests
DS177731CTR	HE4 ControlSet	2 x 1.0 mL/vial
DS177732CTR	CA125 ControlSet	2 x 1.0 mL/vial

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