Try out the online ROMA calculator available on the Elecsys® HE4 page at cobas.com

Download the Roche ROMA application for the iPhone® and the iPad® from the App Store.

Roche ROMA

References

1 Huhtinen, K. et al. (2009). *Br J Cancer.* 100 (8): 1315-1319.
2 Moore, R.G. et al. (2012a). *Am J Obstet Gynecol.* 206: 351.e1-8.
3 Lu, R. et al. (2012). *Biochem. Biophys. Res. Comm.* 419: 274-280.
4 Zhu, Y.-F. et al. (2013). *Asian Pacific Journal of Tropical Medicine. 6*(4): 265-272.
5 Moore, R.G. et al. (2012b). *Scientific Reports.* 4, Article number: 3574.
6 Paulsen, T. et al. (2006). *Int J Gynecol Cancer. 16* (Suppl. 1): 11–17.
7 Bristow, R.E. et al. (2007). *Cancer. 109*:1513–22.
8 Roche HE4 package insert.
9 Ortiz-Munoz, B. et al. (2014). *Tumor Biol.* 35(7):7249-58.
10 Moore, R.G. et al. (2011). *Obstet Gynecol.* 118 (2, Part 1): 280-288.
11 Karlsen, M.A. et al. (2012). *Gynecol Oncol.* 127: 379-383.
12 Patient cases kindly provided by Dr. Rafael Molina, President of ISOBM. Oncology Unit, Laboratory of Clinical Biochemistry, Hospital Clinic, Barcelona, Spain.

The App and the online calculator are for educational use only.

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Assessing ovarian cancer risk with the ROMA algorithm

Combining CA 125 and HE4 tumor markers in pelvic mass evaluation

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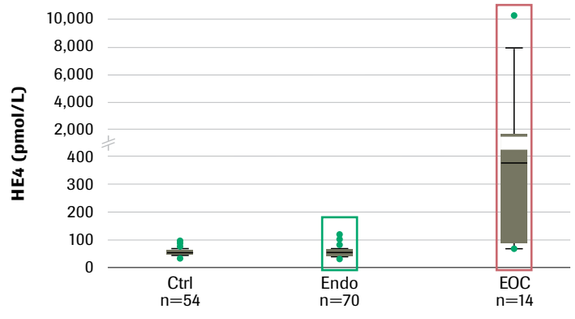
Life needs answers

Introduction of HE4 tumor marker

HE4 level is highly expressed in epithelial ovarian cancer

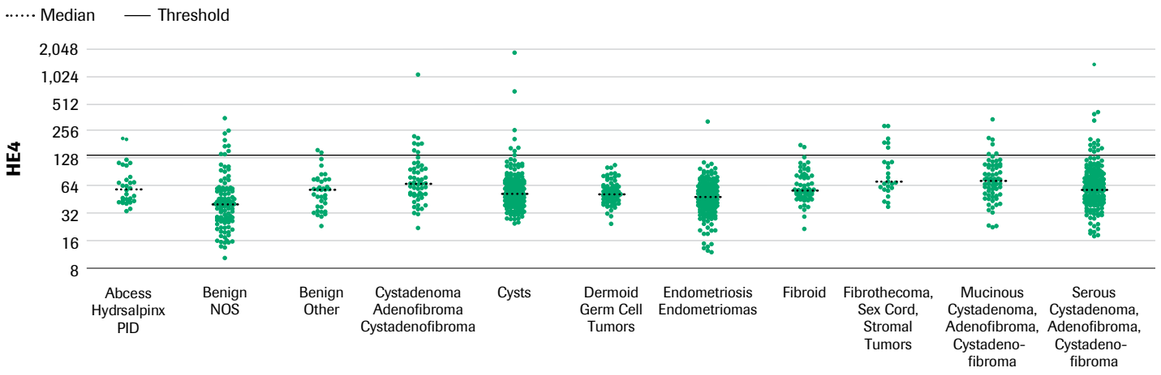
In a study by Huhtinen, K. et al. (2009), serum CA 125 and HE4 concentrations of healthy patients were compared with patients with endometriosis (Endo) and epithelial ovarian cancer (EOC)[1]

- HE4 level is highly elevated in epithelial ovarian cancer
- HE4 shows high differentiation between ovarian cancer vs, endometriosis and healthy controls

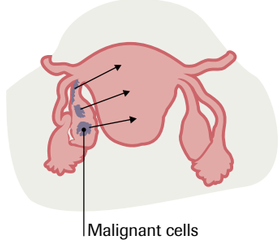


In a study by Moore, R.G. et al. (2012a), serum were obtained from 1,042 women with benign diseases prior to surgery for pelvic mass and HE4 levels were determined.[2]

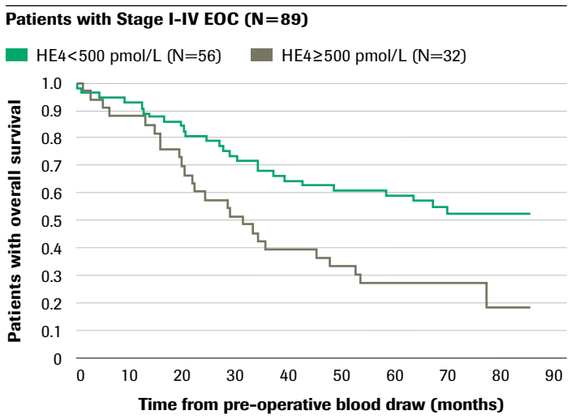
- HE4 levels were in general not elevated in benign diseases, including ovarian cysts and endometriosis



HE4 is involved in ovarian cancer cell proliferation and invasion[3-5]



Patients with high HE4 levels have poorer outcomes, suggesting HE4 plays an important role in ovarian cancer



In a study by Moore, R.G. et al. (2012b), Kaplan-Meier survival curves of 89 ovarian cancer patients (all stages) were shown.[5]

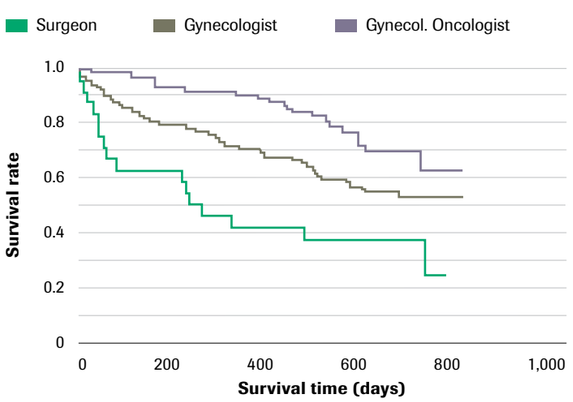
The graph shows decreased survival for patients with HE4 ≥ 500 pmol/L compared to patients with HE4 < 500 pmol/L. Women with high HE4 levels had a 5-year median overall survival of 27 % compared to 59 % for those with low HE4 levels. Hazard ratio = 2.2 (p = 0.005).

Accurate pelvic mass evaluation leads to accurate referral decision

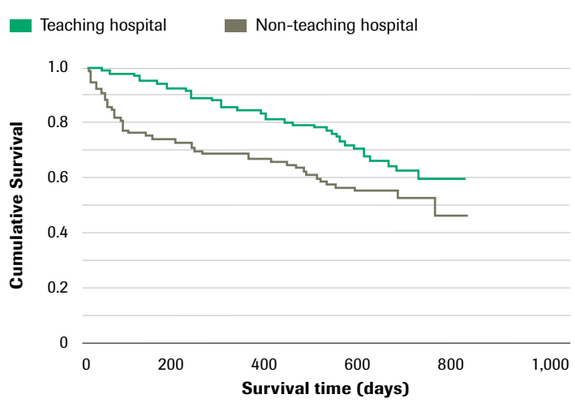
Referral decision impacts patient survival and cost effectiveness of treatments

Survival rate in ovarian cancer patients is dependent on the type and the quality of surgery to remove the tumor as completely as possible. Paulsen et al. (2006) showed that, among 198 women with diagnosis of advanced epithelial invasive ovarian, tubal, and peritoneal cancer, the highest survival rate can be achieved when treatment is done with gynecological oncologists and in expert centers (e.g. teaching hospitals). This improved survival may be because the surgery for ovarian cancer is complicated and gynecological oncologists or specialists at expert centers are trained to perform the comprehensive dubulking and surgical staging needed for optimal treatment of ovarian cancer.[6]

Bristow et al. (2007) showed that referral of patients with ovarian cancer to expert centers was more cost-effective than referral of patients with ovarian cancer to less experienced centers: $9,893 per quality-adjusted life year (QALY) compared with $17,149 per QALY, respectively.[7]



Women who had surgery performed by gynecological oncologists had 20 % increase in short-term survival compared to women who had surgery performed by non-gynecological oncologists ($p<0.0001$).[6]



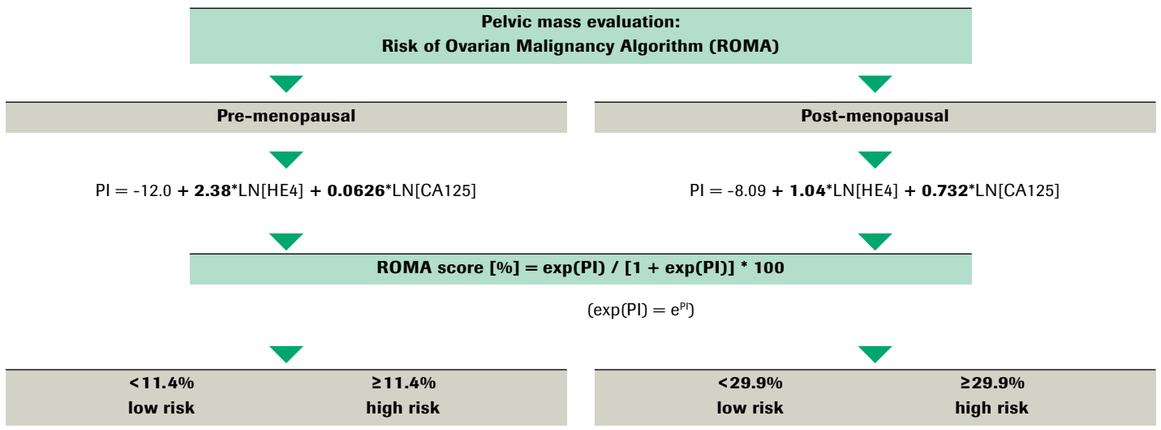
Women who were operated at teaching hospitals had longer survival compared to those who were operated at non-teaching hospitals (Hazard ratio=1.83; p=0.02).[6]

ROMA, Risk of Ovarian Malignancy Algorithm, in pelvic mass evaluation

CA 125 and HE4 can be combined in a mathematical algorithm to better assess the risk of epithelial ovarian cancer in women with pelvic mass

Risk assessment with the ROMA (Risk of Ovarian Malignancy Algorithm) score:
The score is used to calculate the risk of having epithelial ovarian cancer in women arriving at the physician with pelvic mass. It includes the biomarker levels of HE4 and CA 125 and also considers the menopausal status of the woman.

The dual marker combination can be used to classify women into high and low risk groups, allowing for the effective triage of women to appropriate surgical centers for their care.[2,8]

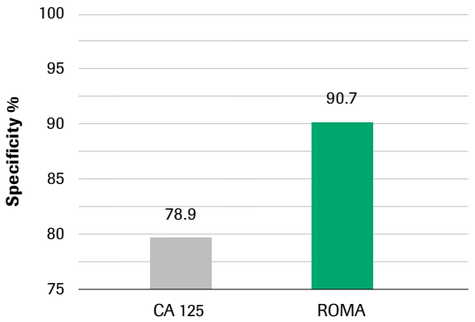


Calculation of the ROMA scores for pre- and post-menopausal women and individual cut-points for the Roche assays to separate between low and high risk patients[9]

Clinical benefits of ROMA

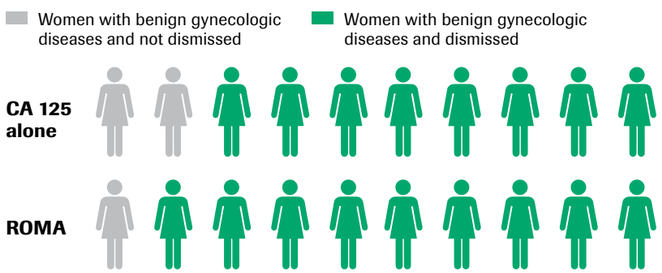
Compared to testing CA 125 alone, ROMA has higher specificity for ovarian cancer detection

Ovarian cancer vs. benign gynecologic diseases



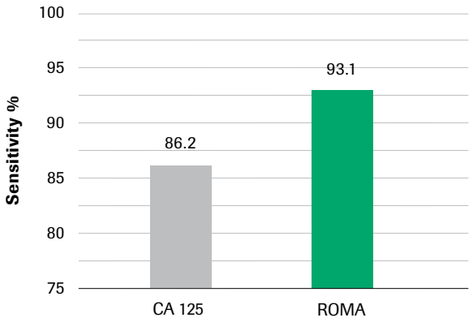
This means …

Among 10 women with benign gynecologic diseases, ROMA dismisses 1 more patient which CA125 alone would include as having ovarian cancer



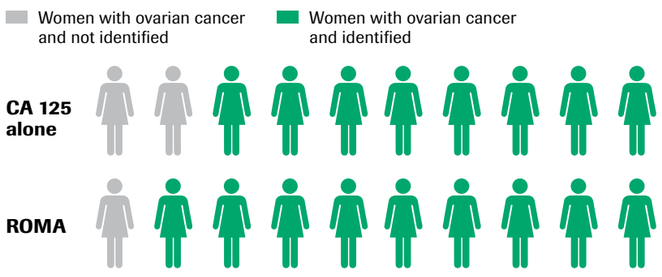
Compared to testing CA 125 alone, ROMA has higher sensitivity for ovarian cancer detection

Ovarian cancer vs. benign gynecologic diseases



This means …

Among 10 women with ovarian cancer, ROMA identifies 1 more patient than CA 125 alone



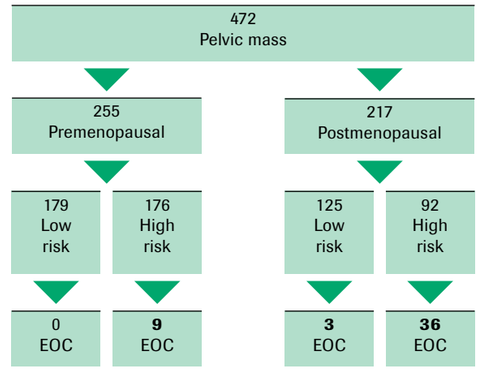
In a study by Ortiz-Munoz, B. et al. (2014), pre-operative serum levels of HE4 and CA 125 were measured in 119 women with benign gynecologic diseases, 67 patients with ovarian cancer and 32 healthy women.[9]

- ROMA has higher specificity and sensitivity than CA 125 alone to discriminate ovarian cancer from benign gynecologic diseases.

ROMA accurately identifies 94% (45/48) of the patients with pelvic mass that have ovarian cancer

In a study by Moore, R.G. et al. (2011), a total of 472 patients were evaluated: 383 women with benign diseases and 48 women with epithelial ovarian cancers (9 pre-menopausal and 39 post-menopausal)[10]

- Use of HE4 and CA 125 with ROMA has a high sensitivity for the prediction of epithelial ovarian cancer in women with pelvic mass



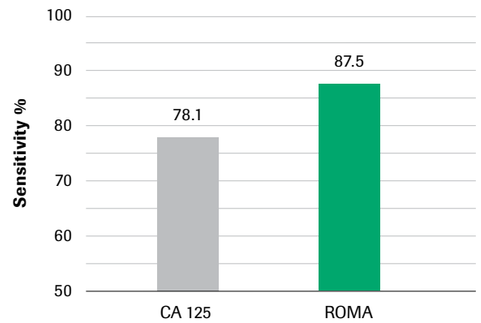
EOC = Epithelial ovarian cancer

Compared to testing CA 125 alone, ROMA increases sensitivity by 10% in the detection of stages I/II ovarian cancer

In a study by Karlsen, M.A. et al. (2012), serum from 1,218 patients in the prospective pelvic mass study was collected prior to diagnosis.[11]

- Diagnosis: 809 benign tumors, 79 borderline ovarian tumors, 252 ovarian cancer (64 early and 188 late stage), 9 non-epithelial ovarian tumors and 69 non-ovarian tumors
- The study concluded that ROMA increases differentiation of ovarian cancer from other pelvic masses than CA 125 alone, even in early stage ovarian cancer
- ROMA might be valuable as a first line biomarker for selecting high risk patients for referral to a tertiary center and further diagnosis

Stages I/II ovarian cancer vs. benign gynecologic diseases



ROMA in action: Patient cases[12]

Patient case #1

A 44-year-old (pre-menopausal) female with abdominal pain and a history of endometriosis was detected by ultrasound to have a pelvic mass. Her test results were the following:

Parameter	Result	Normal interval
Creatinine	0.7	<0.9 mg/dL
AST	22	<35 U/L
ALT	19	<35 U/L
CA 19-9	22	<39 U/mL
CA 125	150	<35 U/mL
HE4	34	<140 pmol/L
ROMA	3.6	<11.4 % for pre-menopausal

Report: High CA 125 level but normal HE4 level
Diagnosis: Endometrial cyst and exacerbation of endometriosis

ROMA score: Low risk
Low risk ROMA score supports the diagnosis of non-malignant tumor

Patient case #2

A 52-year-old (pre-menopausal) female was detected by ultrasound to have a pelvic mass. Her test results were the following:

Parameter	Result	Normal interval
Creatinine	0.7	<0.9 mg/dL
AST	22	<35 U/L
ALT	45	<35 U/L
CA 19-9	6	<39 U/mL
CA 125	19	<35 U/mL
HE4	601	<140 pmol/L
ROMA	96.8	<11.4 % for pre-menopausal

Report: High HE4 level but normal CA 125 level
Diagnosis: Ovarian cancer

ROMA score: High risk
High risk ROMA score supports the diagnosis of ovarian cancer

Patient case #3

A 58-year-old (post-menopausal) female, non-smoker with no toxic habits was referred following the detection of a pelvic mass during an ultrasound scan. Her test results were the following:

Parameter	Result	Normal interval
Creatinine	0.86	<0.9 mg/dL
AST	32	<35 U/L
ALT	23	<35 U/L
CA 19-9	6	<39 U/mL
CA 125	324	<35 U/mL
HE4	467	<140 pmol/L
ROMA	92.6	<29.9 % for post-menopausal

Report: High CA 125 and HE4 levels
Diagnosis: Ovarian cancer

ROMA score: High risk
High risk ROMA score supports the diagnosis of ovarian cancer

Patient case #4

A 59-year-old (post-menopausal) female, non-smoker was found to have a pelvic mass. Her test results were the following:

Parameter	Result	Normal interval
Creatinine	0.9	<0.9 mg/dL
AST	32	<35 U/L
ALT	25	<35 U/L
CA 19-9	16	<39 U/mL
CA 125	29	<35 U/mL
HE4	83	<140 pmol/L
ROMA	26.3	<29.9 % for post-menopausal

Report: Normal CA 125 and HE4 levels
Diagnosis: Ovarian cyst

ROMA score: Low risk
Low risk ROMA score supports the diagnosis of non-malignant tumor