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SPECIALISED MEDICAL PATHOLOGY

HE4/ROMA
and their role in ovarian cancer

THE PATHOLOGIST'S MEMORANDUM

LABORATORY TESTING AND PATHOLOGY

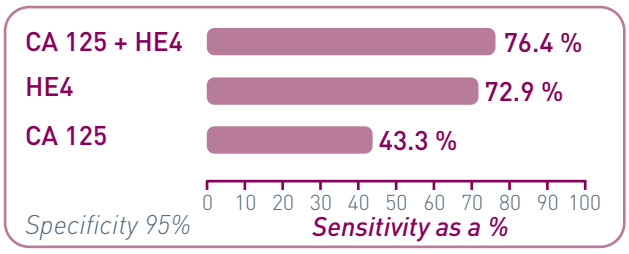
The diagnosis of ovarian cancer relies on clinical examination (abdominal and gynaecological examination) and imaging (scanner, MRI: work-up for extension). The diagnosis is confirmed by tissue sample analysis, which is carried out through laparoscopy or laparotomy.

Diagnosis is often made late due to the clinical examination remaining normal and the symptoms, when present, being unspecific: asthenia, weight loss, change in general health, back pain, feeling of abdominal bloating, abdominal pain and an urgent need to urinate. Patient survival is directly linked to how early the diagnosis is made.

In terms of laboratory testing, the main marker is the CA125 serum marker, however, it is low in specificity and sensitivity.

The CA125 assay is not recommended for the screening of ovarian cancer. According to the French National Authority for Health (HAS), an initial profile screen is recommended, as well as monitoring and follow-ups of patients with ovarian cancer.
HE4 (Human Epididymal Protein) is a glycoprotein that belongs to the WFDC2 (Whey Acidic Four Disulphide Core protein) family, previously the WAP gene family, which includes protease inhibitors.

Even in the first stages of ovarian cancer (stages I and II), HE4 is over-expressed and mainly found in serous, endometrial and clear-cell cancers. Its expression is independent of CA125 and it is effective in 50% of cancers that do not express CA125.



HE4 is more sensitive and specific than CA125 and when combined they offer a better detection sensitivity for early-stage ovarian cancers and cancer recurrence (Moore RG et al. Gynecol Oncol 2008).

ROMA™ algorithm: Risk of Ovarian Malignancy Algorithm (%)

The ROMA algorithm assesses the risk of malignancy by combining the serum HE4 result, the CA125 result and the menopausal status.

It allows patients to be classed according to their risk of malignancy level, i.e. low or high, by taking into account their menopausal status. In a study by Moore RG (Gynecol Oncol 2009), this risk was correctly evaluated for 93.8% of patients.

INDICATIONS FOR TESTING

- Assistance in the early diagnosis of ovarian cancer,
- Stratification of the risk in a woman with a pelvic mass or ovarian cyst. - Follow-up of women with ovarian cancer: detection of cancer recurrence.

ASSAY TECHNIQUE

Electrochemiluminescence, on the Cobas® analyser by Roche.

For the ROMA algorithm, HE4 and CA125 must be measured using the same methodology, one which does not authorise the integration of a transferred CA125 result. The menopausal status must be **indicated. The test request must specify "ROMA calculation" in order for it to be carried out.**

INTERPRETATION

- **In pre-menopausal women:**

ROMA ≥ 11.4 = high risk of ovarian cancer
ROMA < 11.4 = low risk of ovarian cancer

- **In post-menopausal women:**

ROMA ≥ 29.9 = high risk of ovarian cancer
ROMA < 29.9 = low risk of ovarian cancer

For the detection of ovarian cancer: HE4 outperforms CA125. It is more sensitive and more specific (notably, it is not raised in cases of endometriosis). However, this marker is not totally specific to ovarian tissue, or ovarian cancer: it is over-expressed in thyroid cancers, salivary gland cancers and endometrial cancers. In addition, its expression is high to moderate in cases of pulmonary adenocarcinomas, mammary adenocarcinomas and mesotheliomas.

In patients with a pelvic mass or an ovarian cyst, the ROMA calculation is a better way of evaluating the risk of cancer. It enables the number of unnecessary surgical interventions to be reduced, and in return, means that women with a raised risk can be sent to a specialised team.

Following-up on patients with ovarian cancer: HE4 is useful mainly in the cases where the CA125 result sheds no additional light on the case. It's serum concentration increases 2 to 5 months before a clinical recurrence.

SAMPLE REQUIREMENTS

Collect a serum sample: 1 mL is required, the minimal acceptable volume is: 600 µL.
The serum must be separated from the blood cells then **frozen**.

CONTACT DETAILS

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