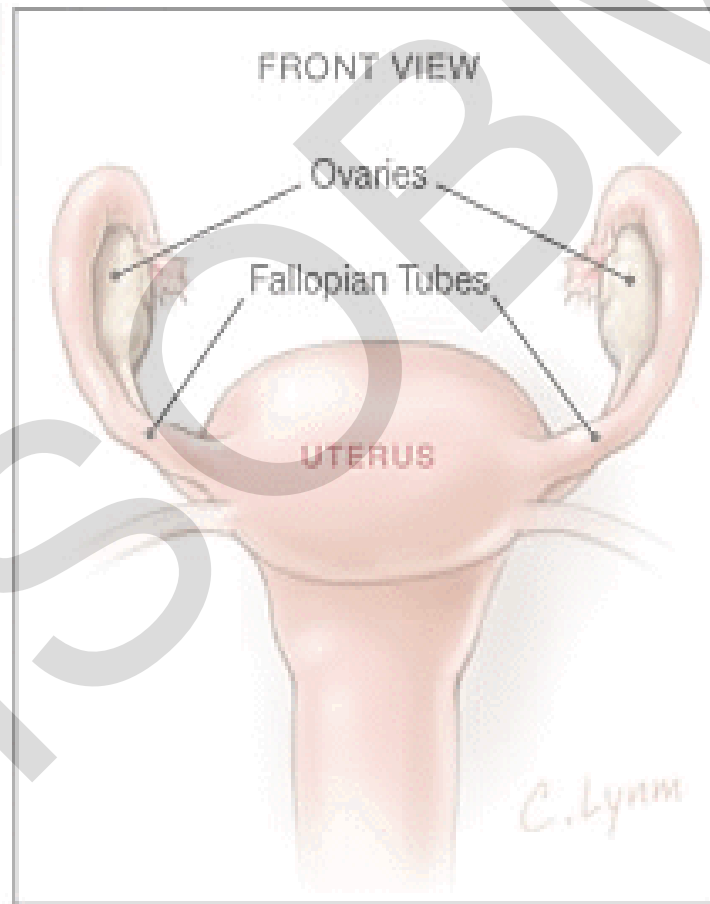


# HE-4 Un nuevo marcador de interés en el diagnóstico del Cáncer de Ovario



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# EGTM GUIDELINES

**New tumor marker... to compare with the Tumor marker of choice in this malignancy**



CA 125

HE-4

**Ovary...Other situations...Falses + Tumor marker distribution**

# OBJETIVES

- 1) To evaluate the HE4 serum levels in healthy subjects and in patients with benign and malignant diseases of various origins.
2. To compare the HE4 clinical utility in comparison with the tumor marker of choice in ovarian cancer, CA 125.

**METHODS** 1059 people;

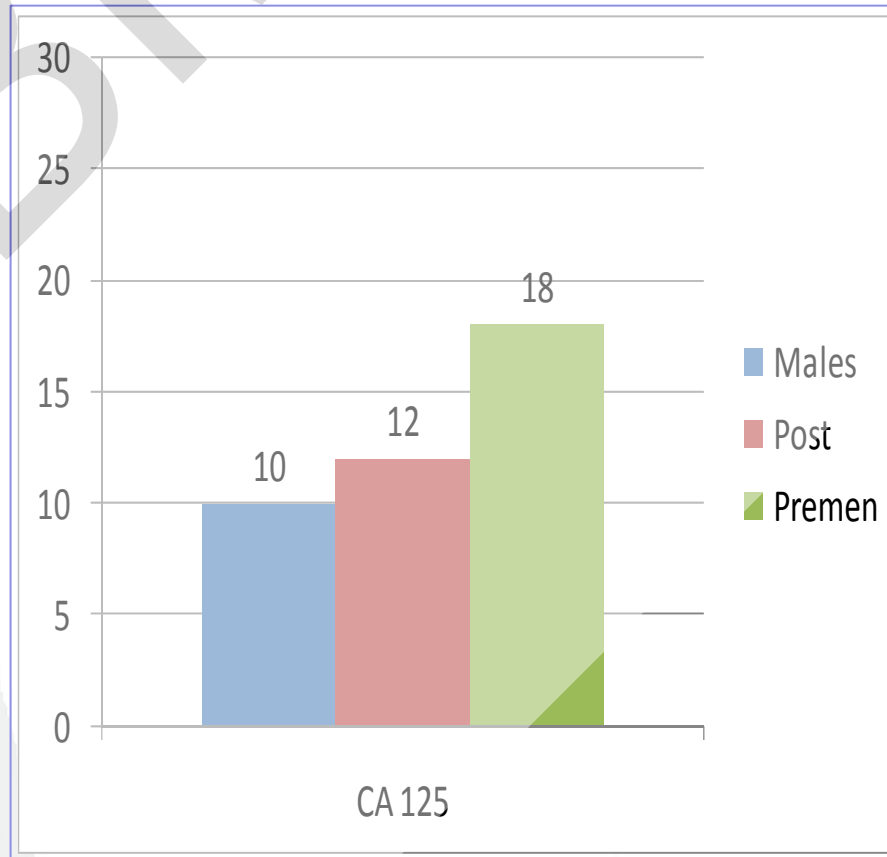
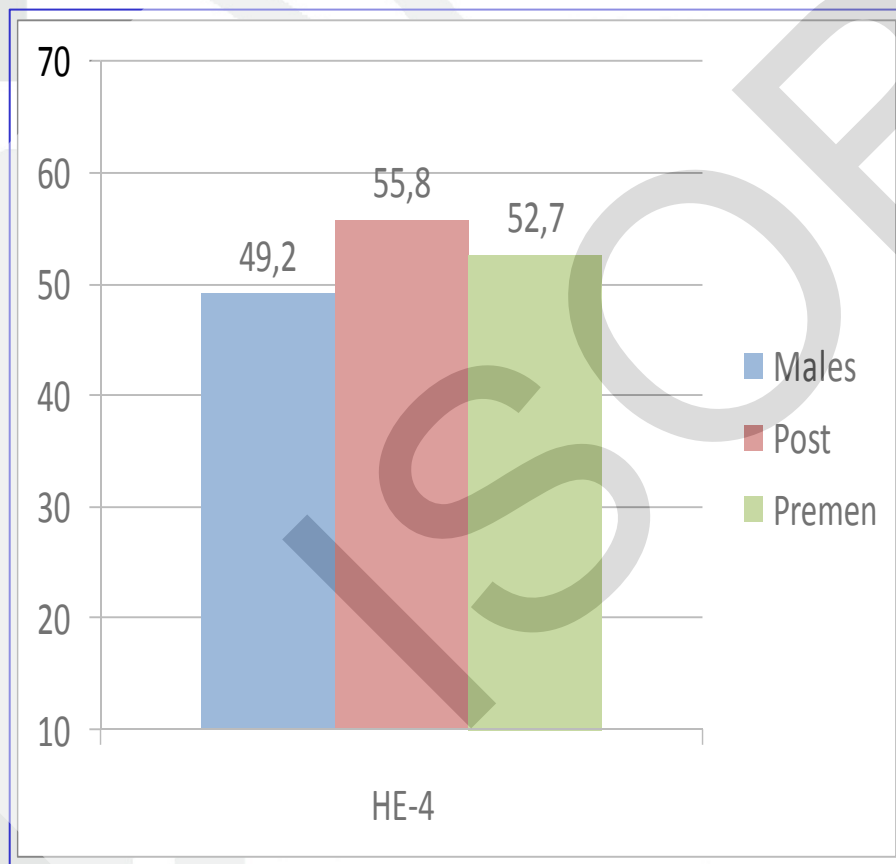
101 HEALTHY	535 BENIGN DISEASES	423 MALIGNANT DISEASES
	<p>22 RENAL FAILURE            81 HEPATIC DISEASE            17 DERMATOLOGICAL            17 CARDIAC            57 LUNG            28 GASTROINTESTINAL            21 AUTOINMUNE            11 OTHERS</p>	<p><u>224 EPITHELIAL NON GYNAECOLOGICAL:</u>            •15 PRIMARLY LIVER CANCER            •56 GASTROINTESTINAL M1            •19 BREAST CA. M1            •14 UROLOGICAL CA.M1            •49 NSCLC            •28 SCLC</p> <p><u>30 HAEMATHOLOGICAL</u>  <u>9 MELANOMA, STAGE IV</u>  <u>5 SARCOMAS M1</u></p>
	<p>66 ENDOMETRIOSIS            58 MYOMAS            144 OVARIAN CYSTS            13 POLYPS            13 OTHERS</p>	<p><u>199 GYNAECOLOGICAL CANCER:</u>            •127 OVARIAN CANCERS            •35 ENDOMETRIAL CA.            • 15 ENDOCERVICAL            •18 SQUAMOUS CERVICAL</p>

# Relation to menopausal status or gender

HE-4 pmol/L

Median

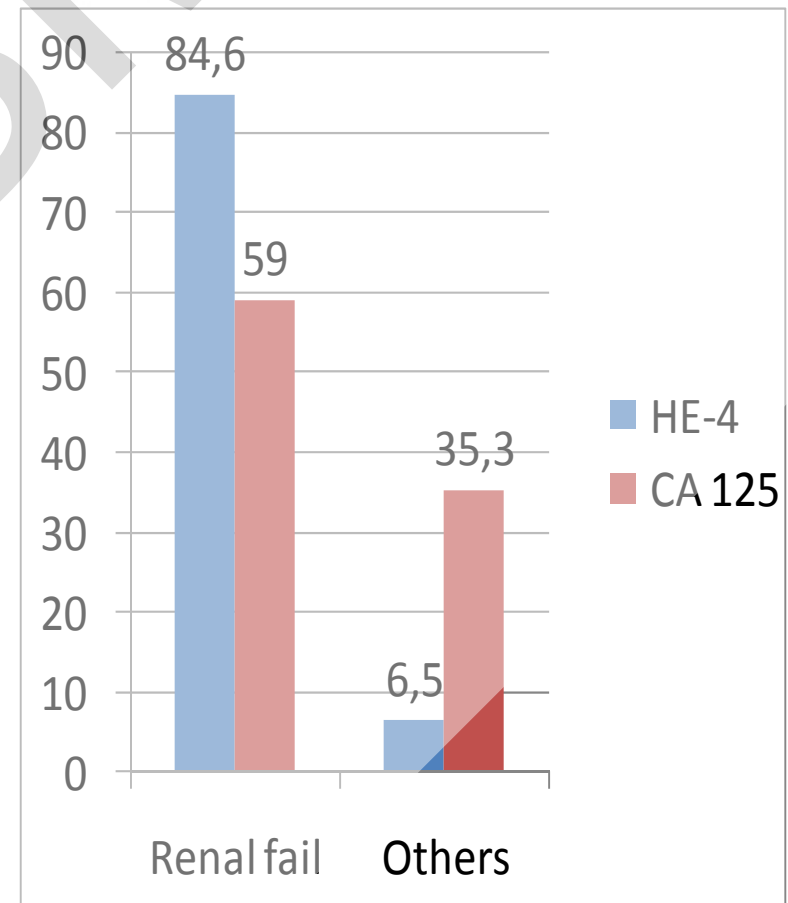
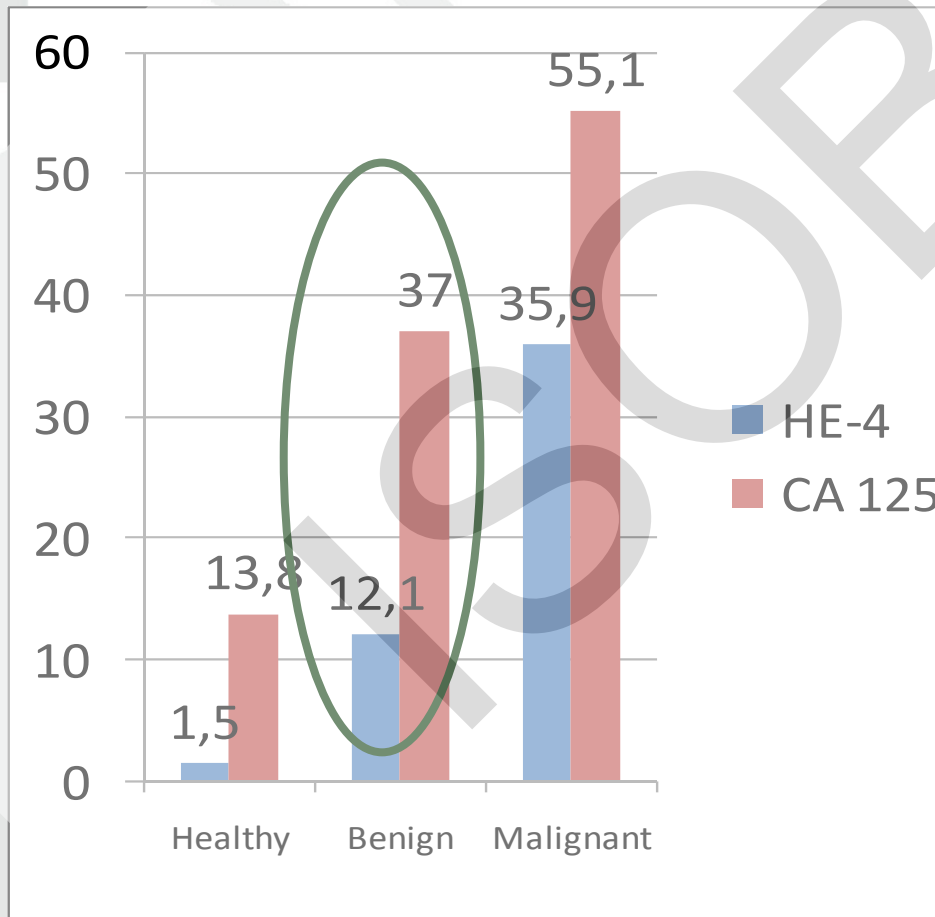
CA 125 ng/ml



**p=0.004**

# HE-4 and CA 125 in benign diseases

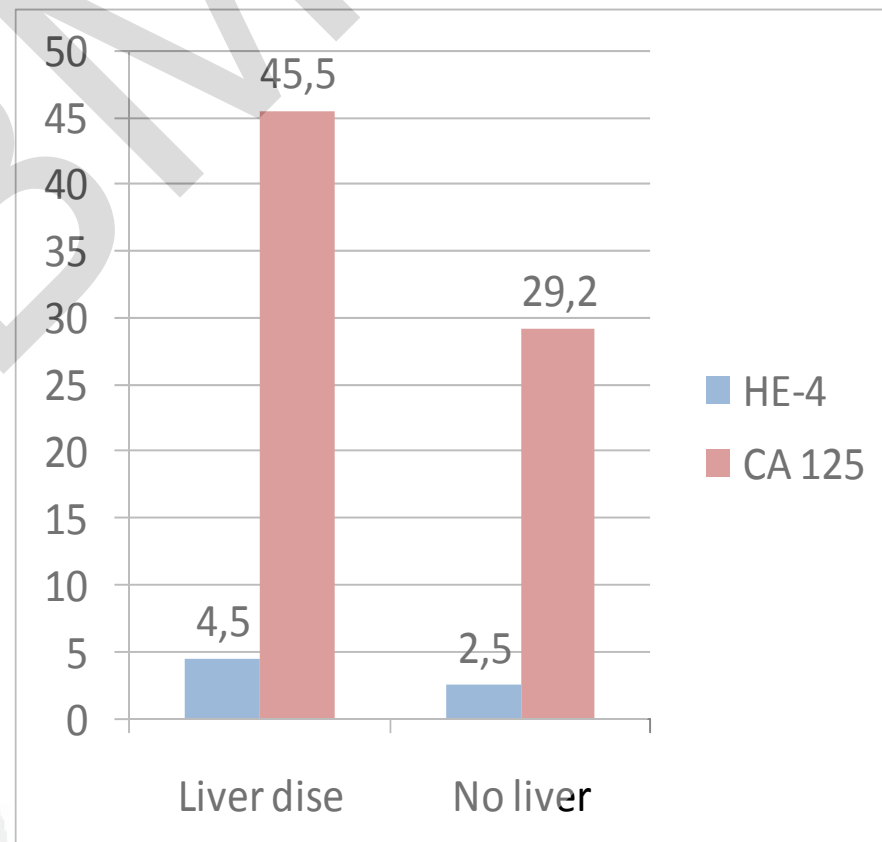
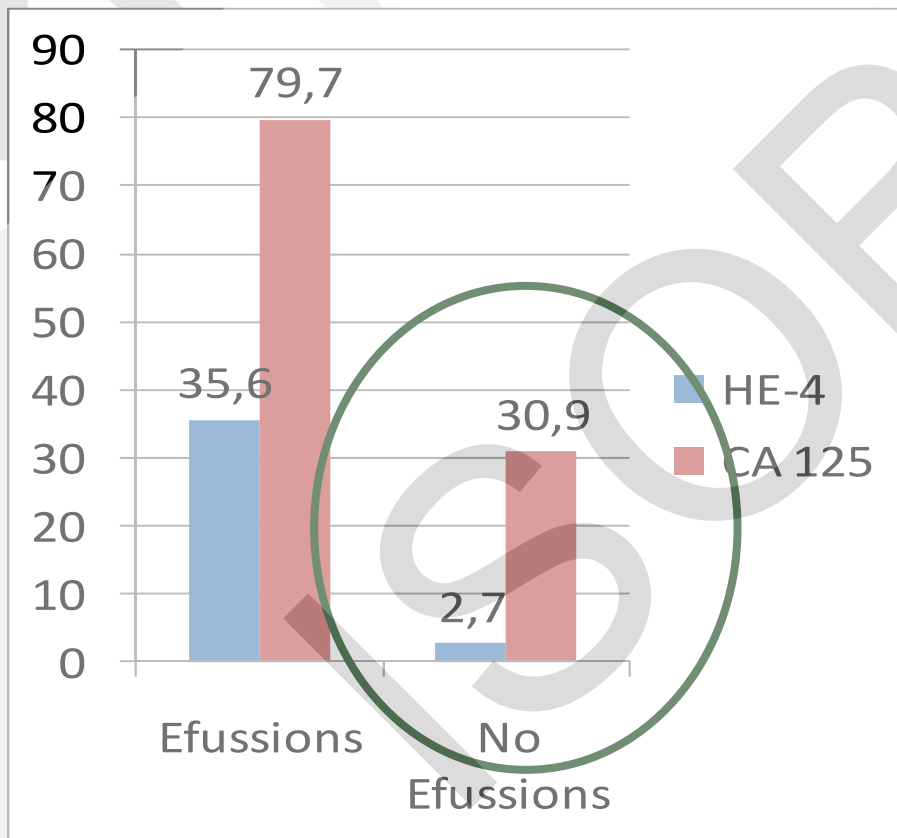
% patients with abnormal values



**HE-4 in renal failure range 20-1000 pg/ml**

# Excluding renal Failure. Benign diseases

% patients with abnormal values



**P=0.001**

**HE-4: 95 Percentile 425 pg/ml**

**HE-4: 95 Percentile 151 pg/ml**

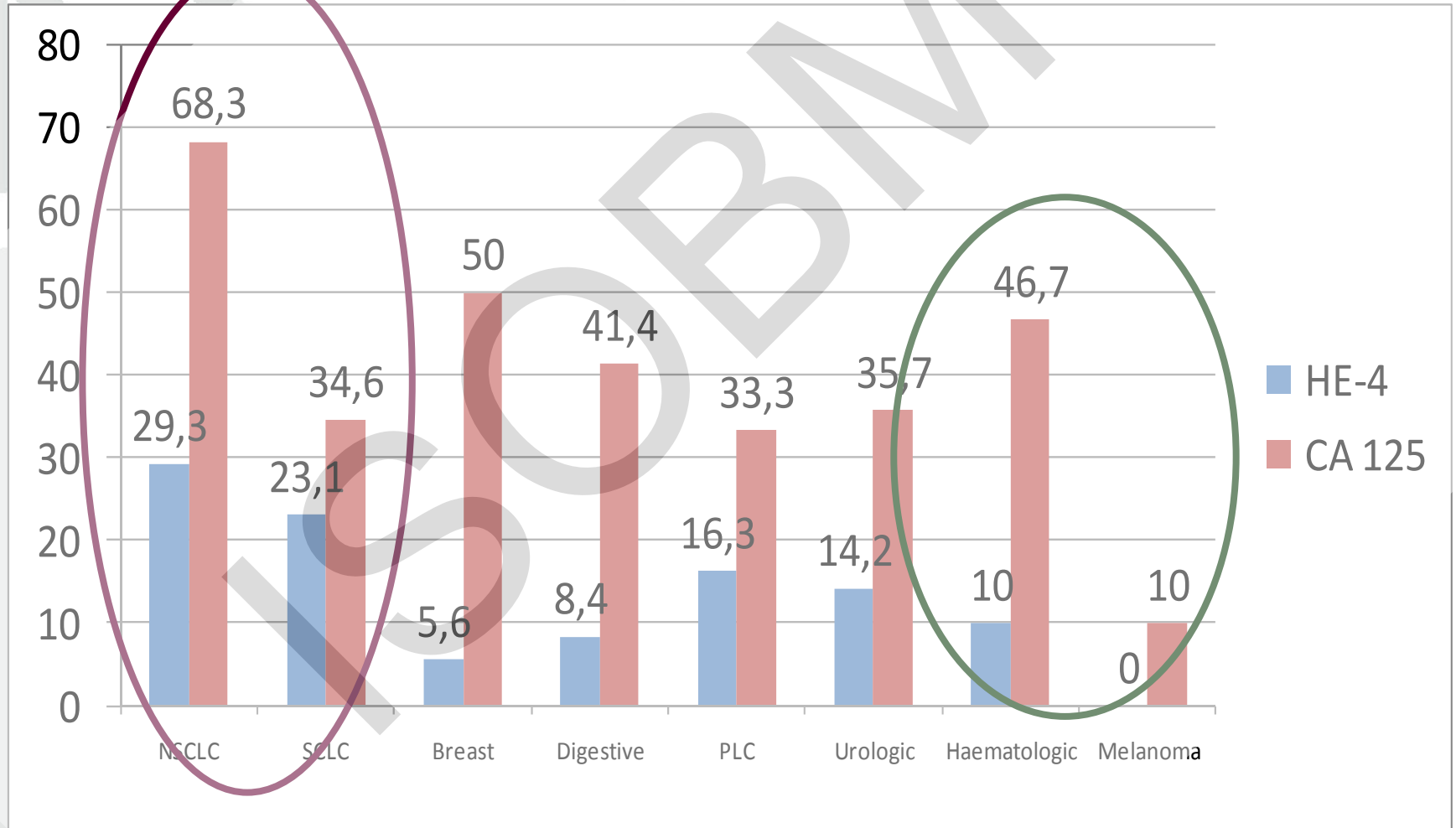
# HE-4

- Higher specificity than CA 125
- To exclude renal failure
- False positive
  - Effusions < 450 pmol/L)
  - Slightly high in 4% of Liver diseases (200 pmol/L)



# % Abnormal values (False positive?) in Non gynaecological malignancies

% patients with abnormal values



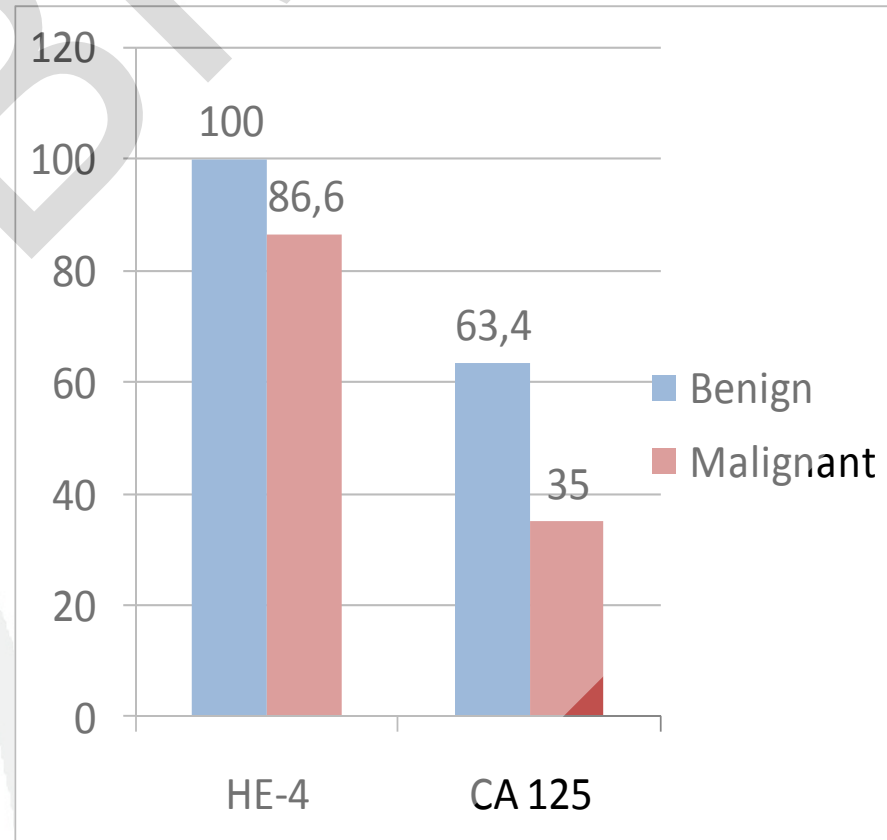
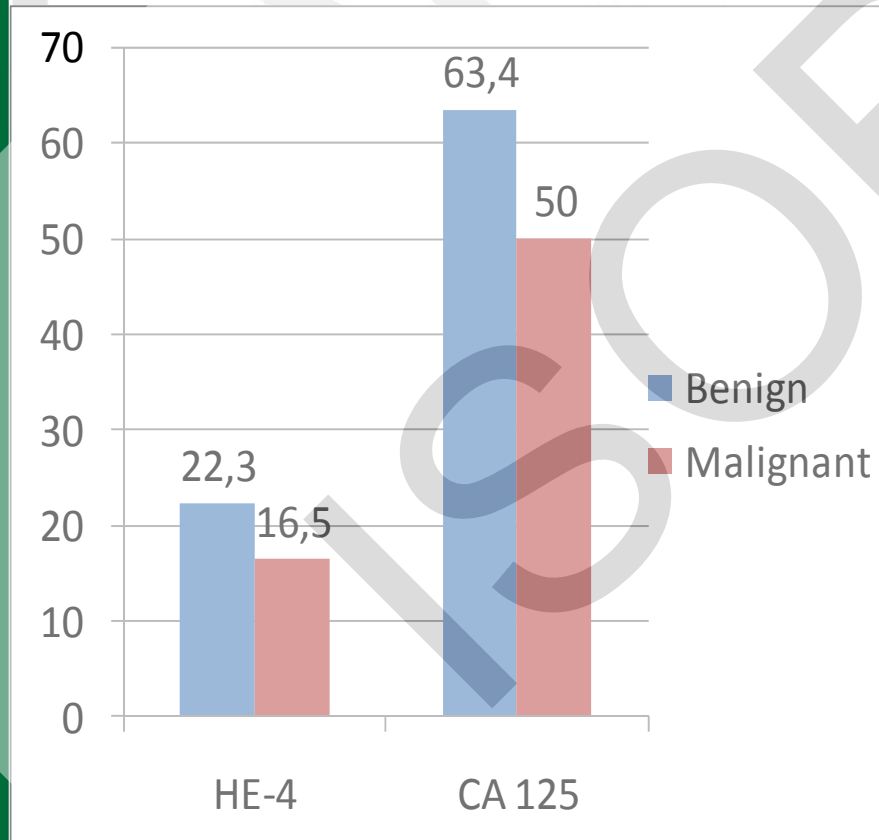
Excluding NSCLC and gynaecological tumors  
95 percentil 215 pmol/L (CA 125 350 U/ml)



# Comparison Benign/malignant with effusions or Liver diseases (excluding NSCLC and gynecological Tumors)

% abnormal values

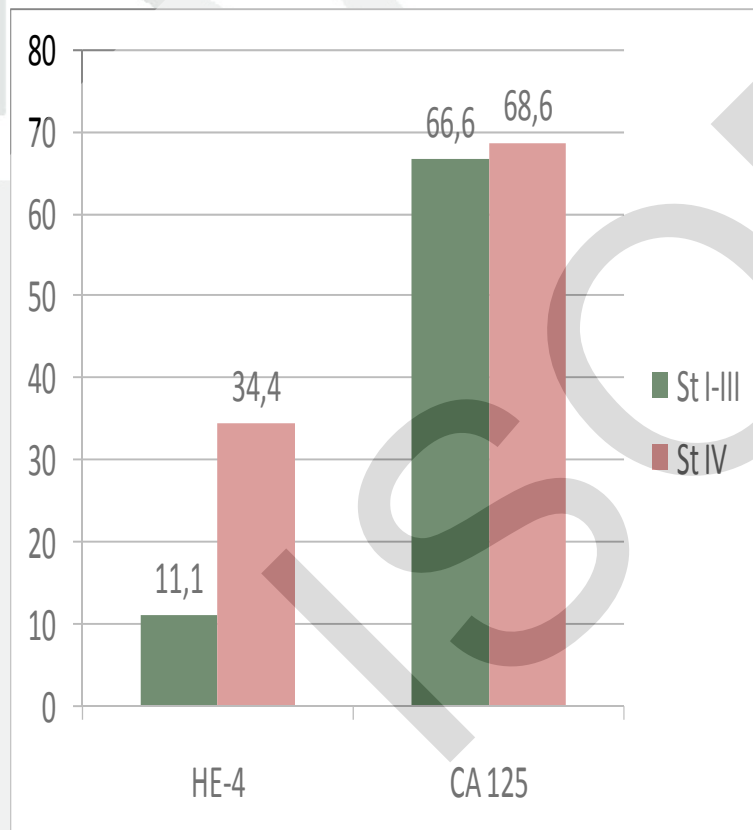
Median concentrations



**Tumor markers are not release by malignant cells**

# Tumor markers in Lung cancer

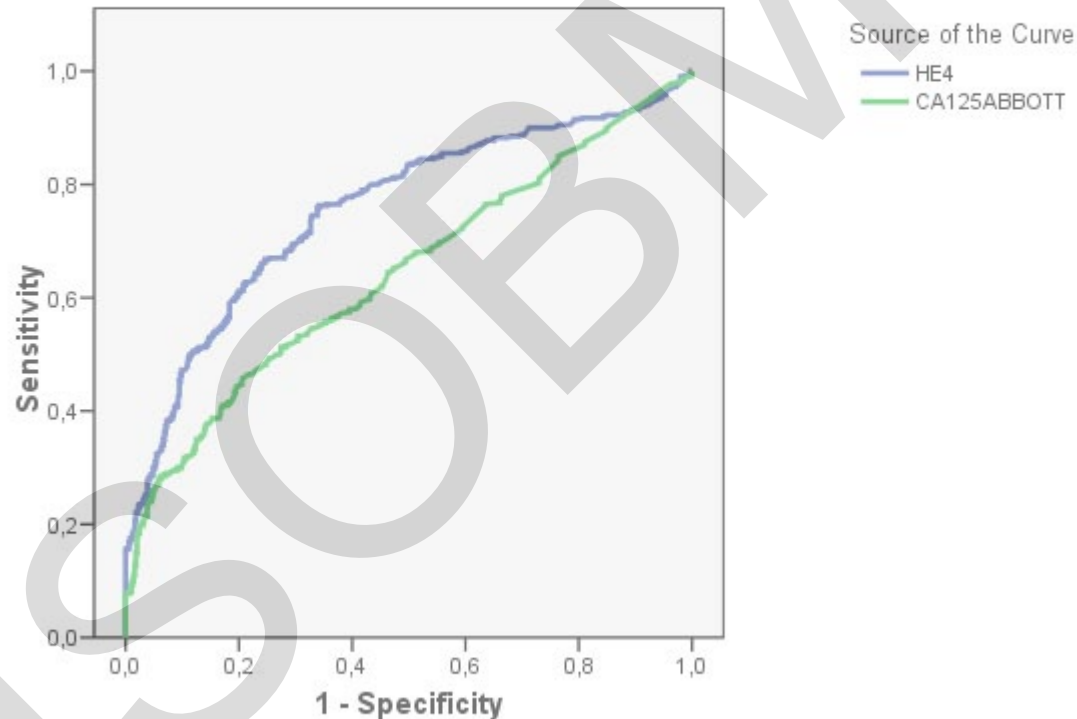
% patients with abnormal values



Percentile 95: 650 pg/ml

# Comparison Benign/cancer, excluding Renal failure

## ROC Curve



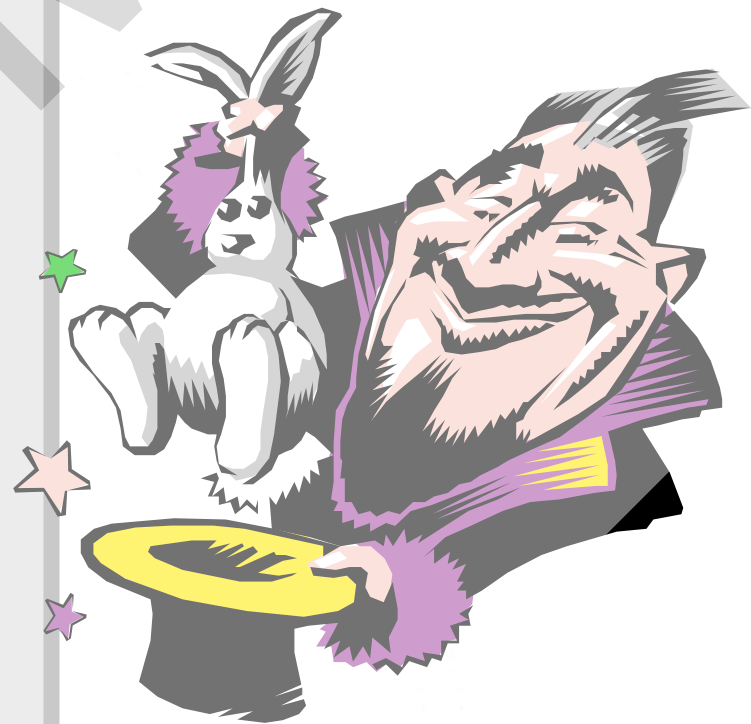
Diagonal segments are produced by ties.

Case Processing Summary	
DIAGNOSTIC	
Positive	400
Negative	496

Area Under the Curve	Area
HE4	,755
CA125ABBOTT	,643

# HE-4 Conclusions 2

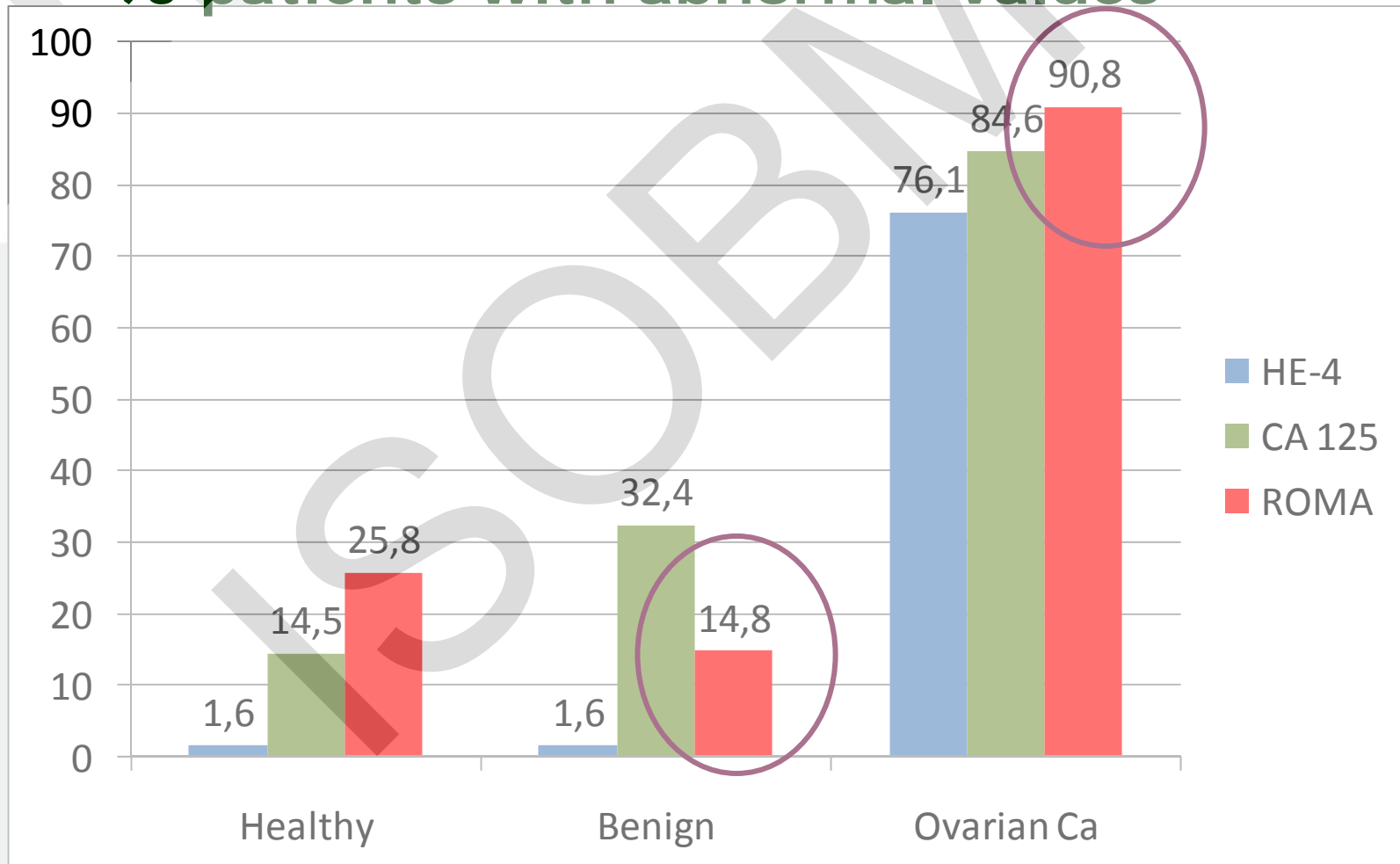
- Abnormal values in Lung cancer and Gynaecological adenocarcinomas.
- HE-4 higher specificity in relation to tumor origin than CA125
  - Slightly increases in Patients with effusions or liver metastases



# Gynecological diseases

(299 benigns, 121 patients with ovarian cancer)

## % patients with abnormal values

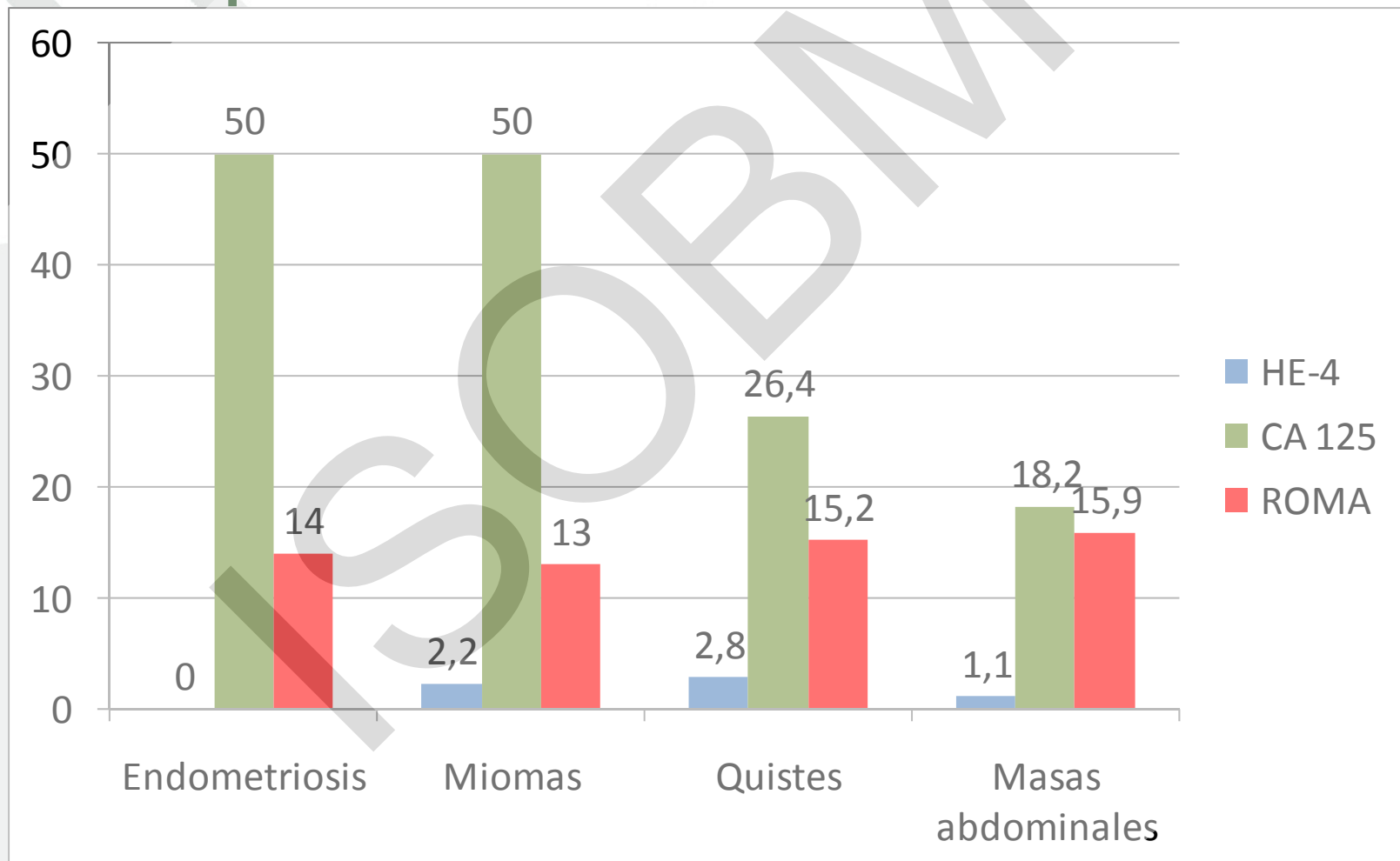


HE-4+.....high risk (>95%)

HE-4-.....ROMA +..... Risk 50%

# Comparison HE-4, CA 125, ROMA

% patients with abnormal values



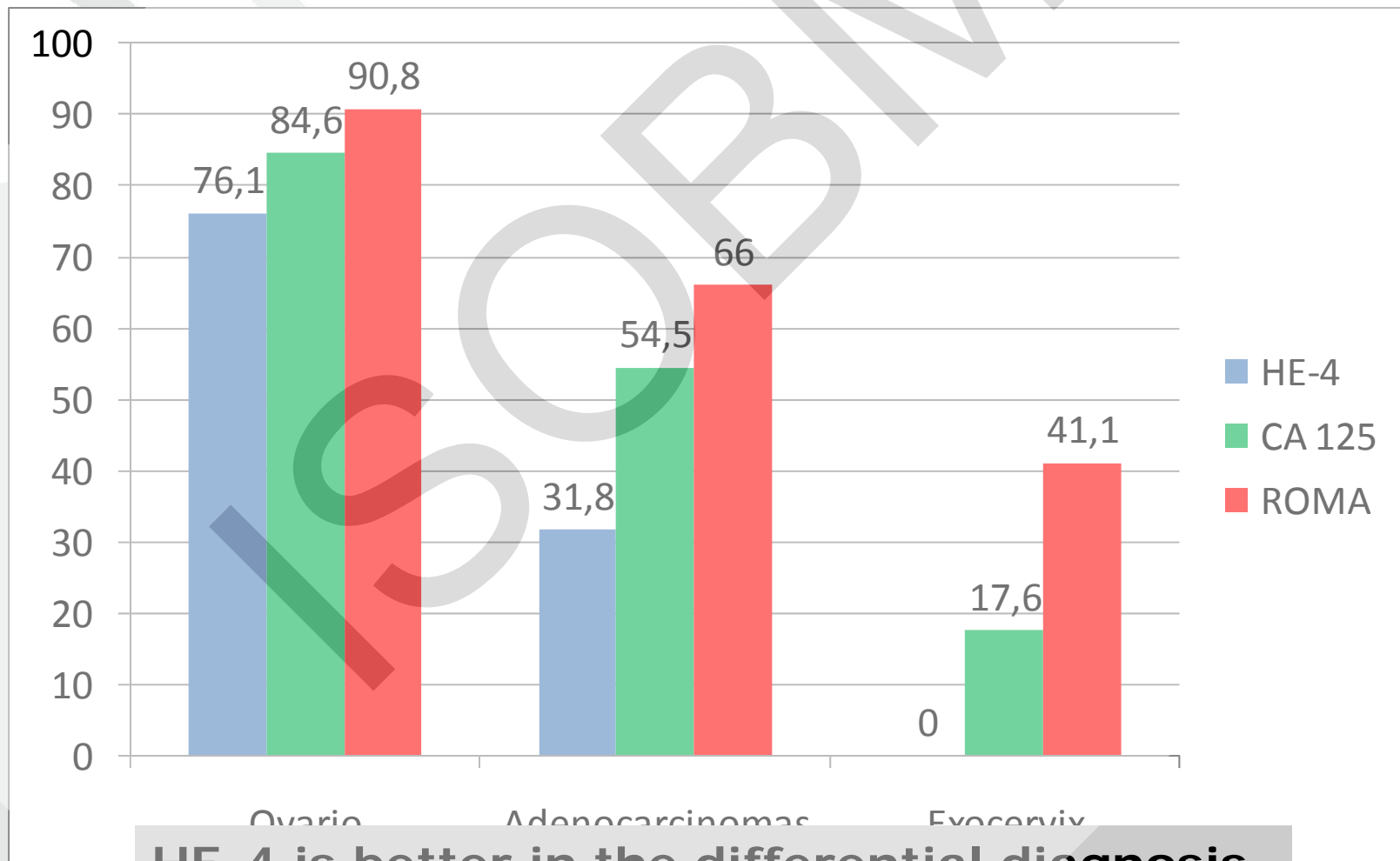
N: 65

56

81 patients

# Comparison HE-4, CA 125, ROMA

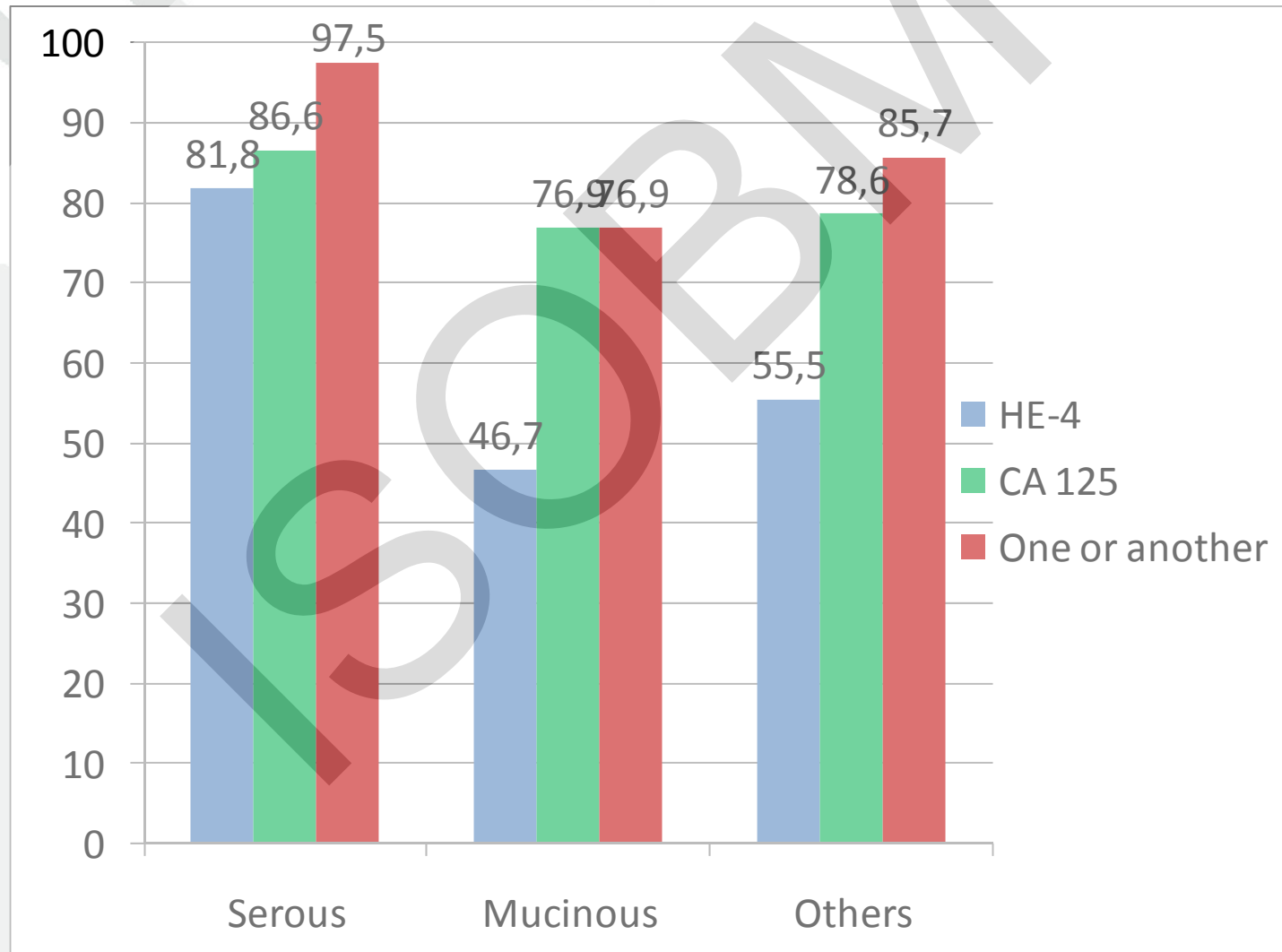
% patients with abnormal values



**HE-4 is better in the differential diagnosis**

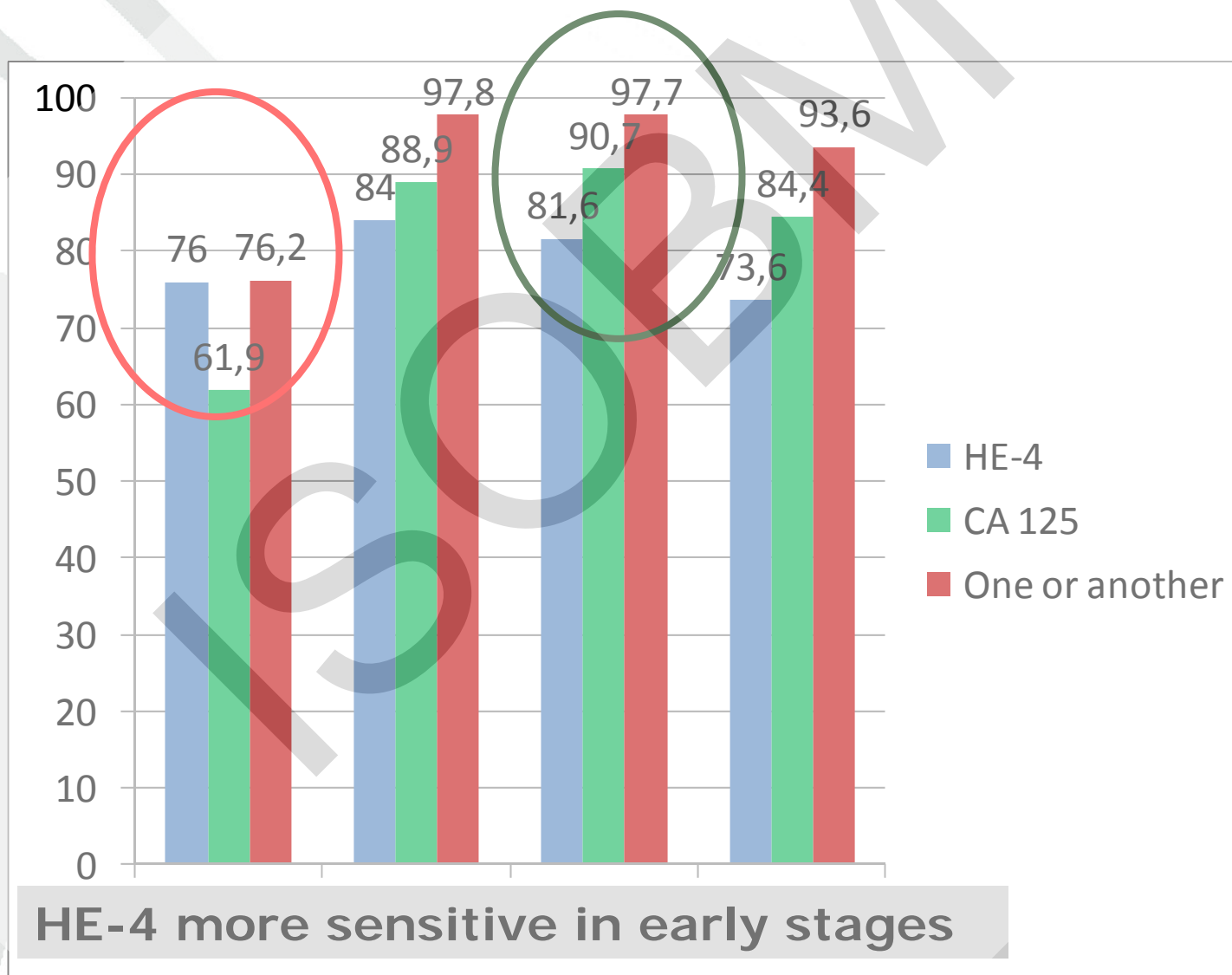
# Ovarian cancer. Histological type

## Sensitivity



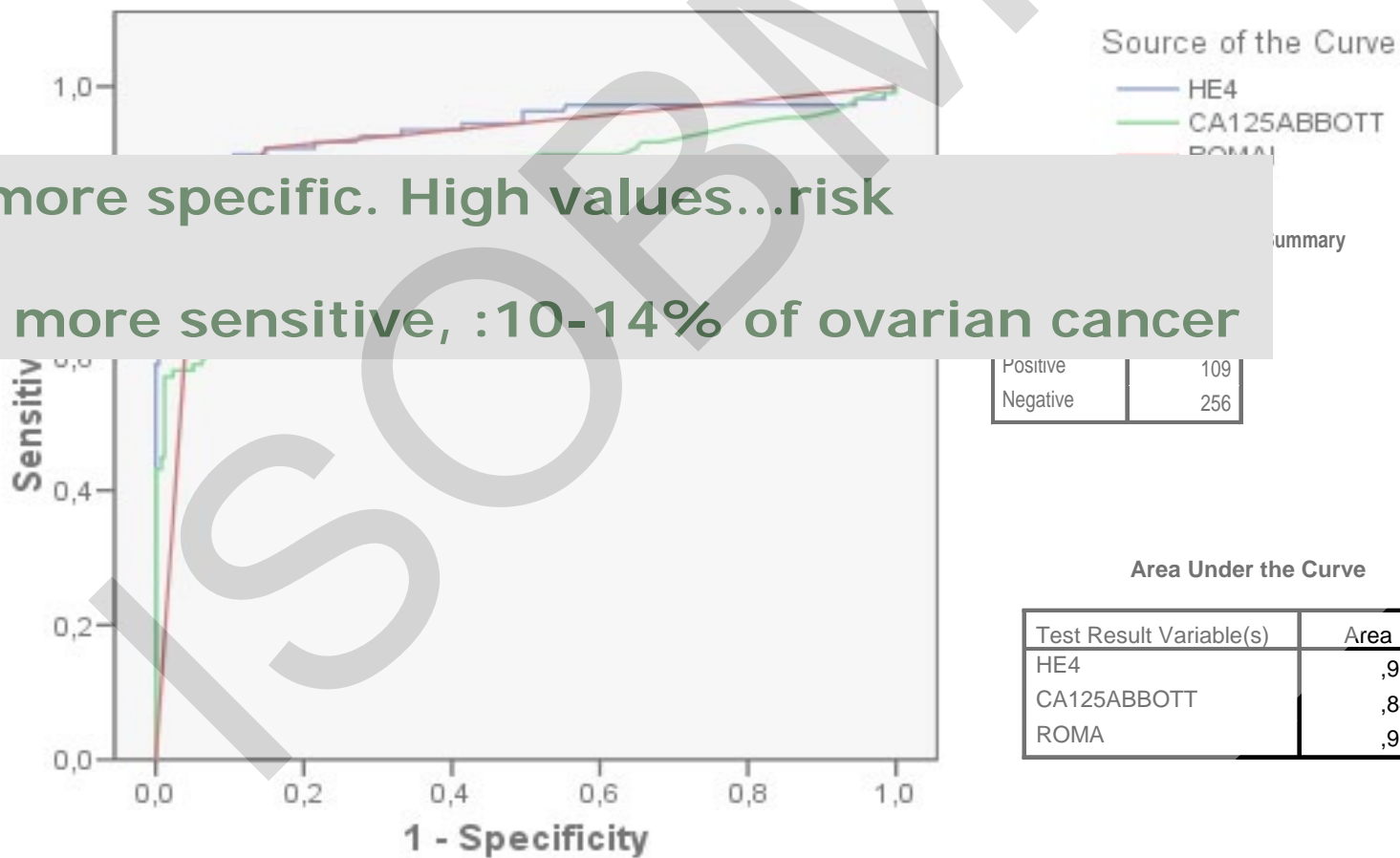
# Ovarian Cancer. Stage

## Sensitivity



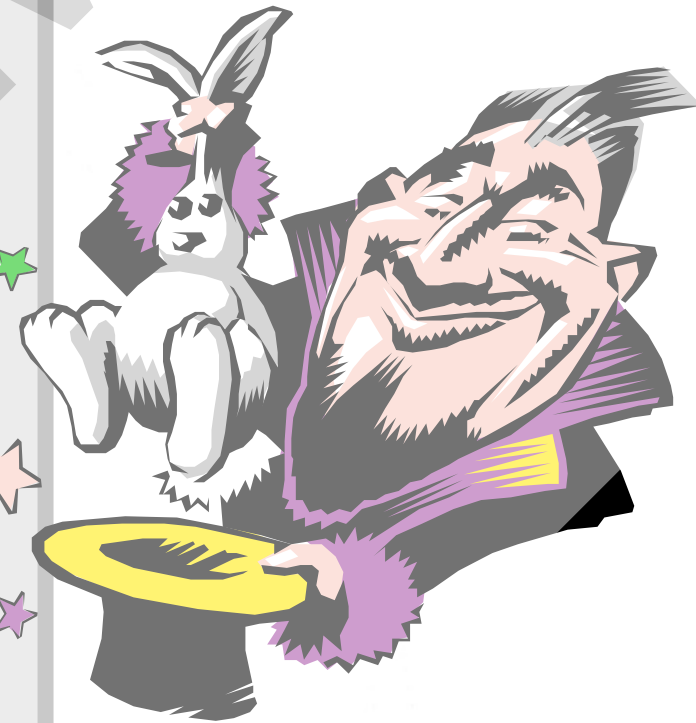
# ROC CURVE BENIGN GYNAECOLOGICAL/ OVARIAN CANCER

ROC Curve



# HE-4

- HE-4 is more specific in gynecological diseases
- HE-4 more sensitive I-II
- CA 125 in III-IV
- Both related to stage and histology
- Combination increase sensitivity





# ROMA

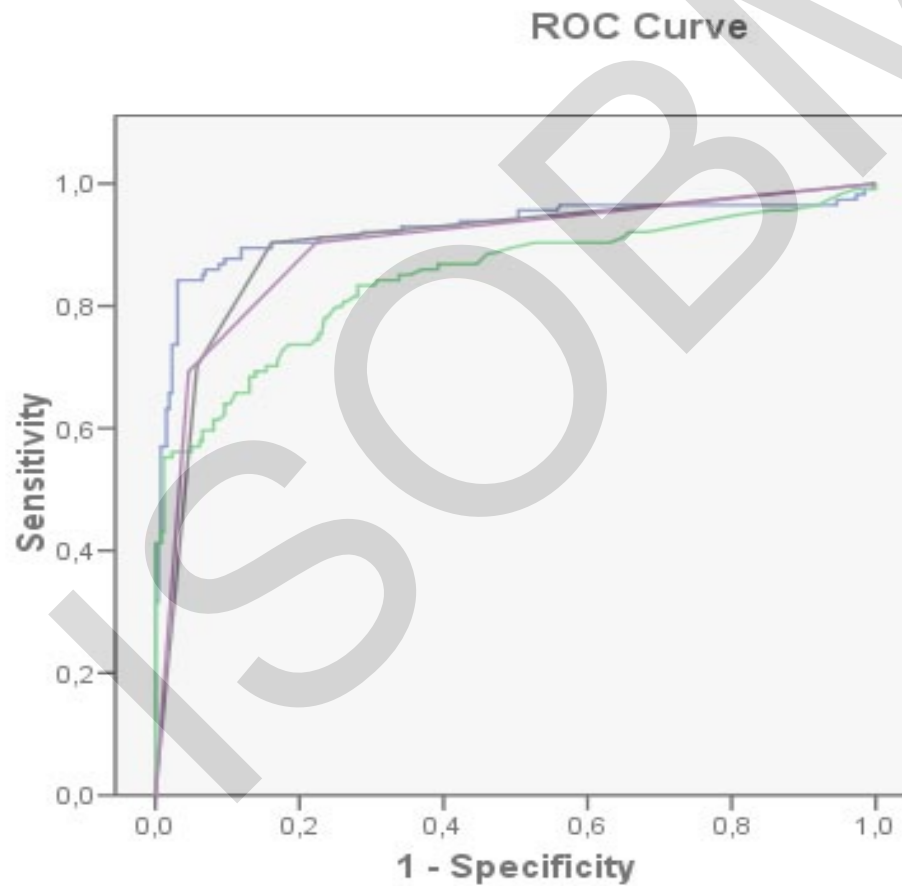
**Mathematical  
model  
Selected  
population.**



**BARCELONA/  
CHICAGO**



# COMPARISON WITH LOCAL ROMA



Source of the Curve

- HE4
- CA125ABBOTT
- ROMA
- MOLINAROMA

Area Under the Curve

Test Result Variable(s)	Area
HE4	,926
CA125ABBOTT	,846
ROMA	,902
MOLINAROMA	,897

Case Processing Summary

	Valid N (listwise)
ginecologico	
Positive	114
Negative	260

# CONCLUSIONS

- HE-4 specificity is higher than CA 125, mainly in patients without renal failure and in patients with gynecological diseases.
- HE-4 is the tumor marker of choice in ovarian cancer and CA 125 is a complementary tumor marker. The combined use, increase the sensitivity obtained in ovarian cancer.
- ROMA increases the sensitivity obtained with HE-4 and CA 125 in the differential diagnosis of abdominal masses, but HE-3 is more specific.