



**Evaluation of oestrogen and progesterone receptor status in HER positive breast carcinoma and correlation with outcome.**

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# INTRODUCTION

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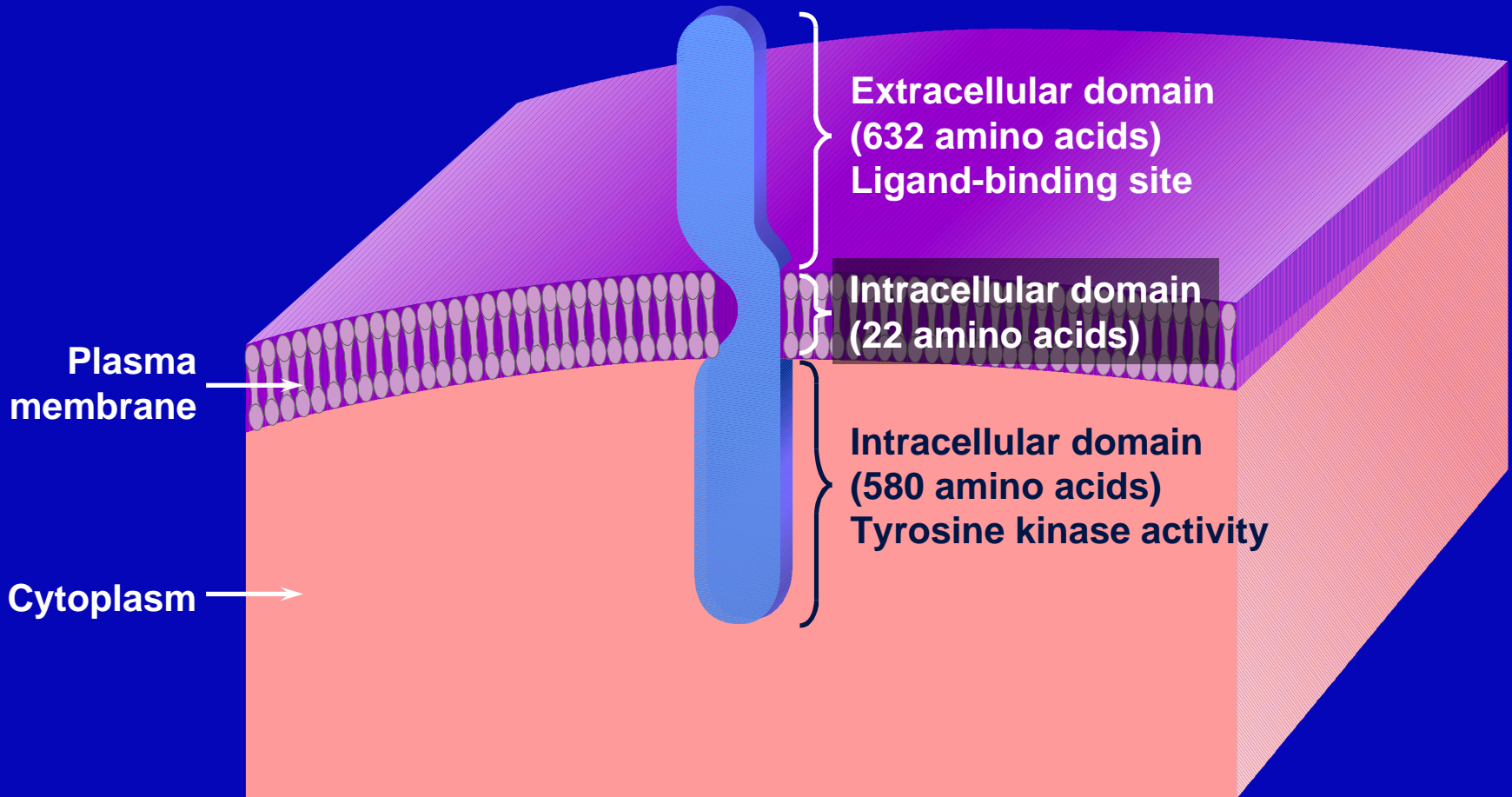
- **HR and HER2:thérapeutic targets having a major impact on the strategy for breast cancer**
- **Determination of their status: mandatory for the TRT and the establishment of the PC.**
- **HER2:is a important prognostic and predictive factor.**
- **HER2:is a specific therapeutic target**

# HISTORY AND TERMINOLOGY

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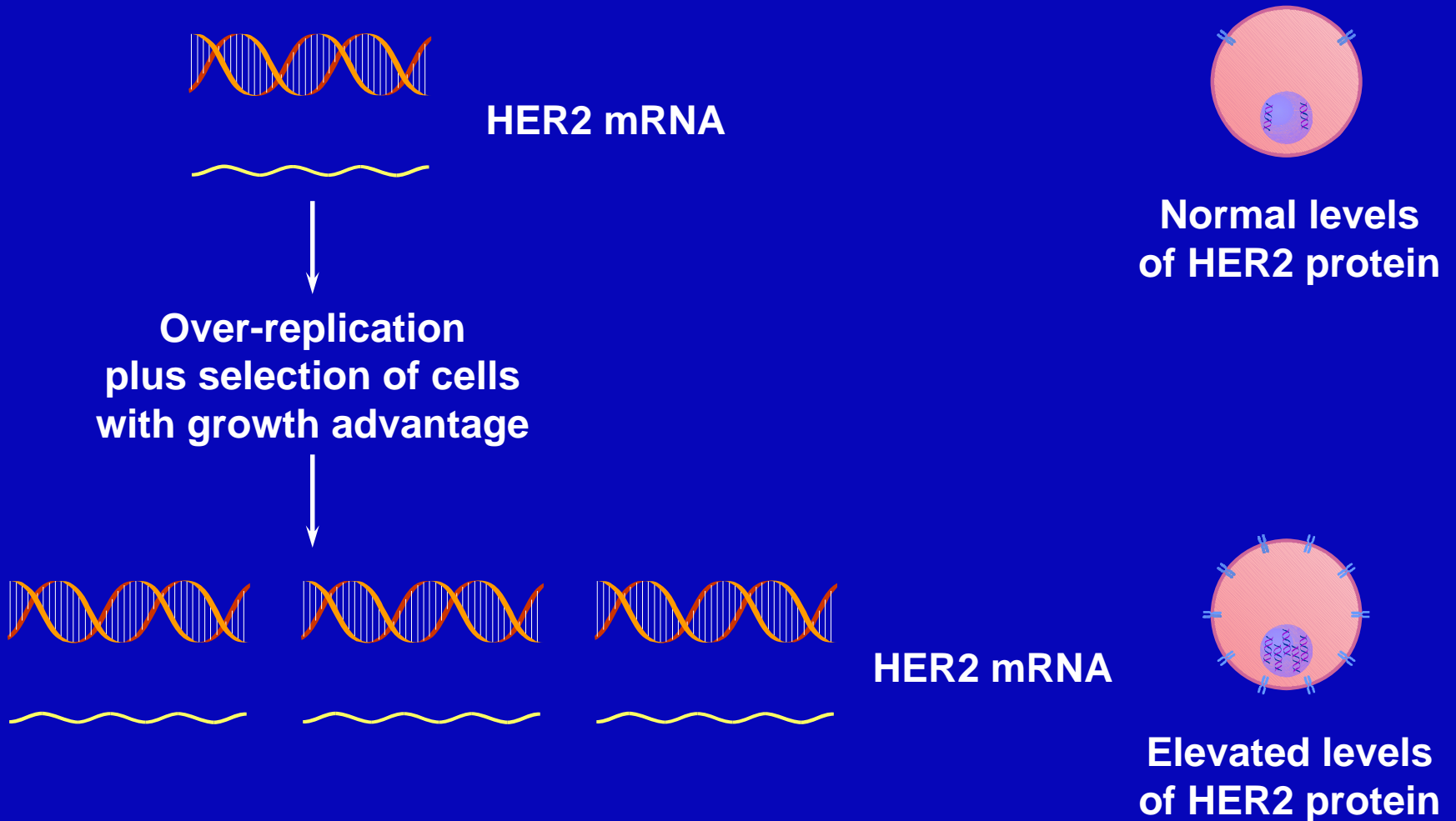
- HER2 was discovered by his counterpart EGF
- HER2=**H**uman **E**pidermal Growth Factor **R**eceptor-**2**
- HER2=c-erb-2 =HER/neu
- Highlighted for the 1st time in rats as Protooncogène
- The mutant gene → activated form → transform cells
- HER2 encodes a transmembrane tyrosine kinase receptor
- Intervenes in growth, division and differentiation

# Transmembrane structure of HER2 monomer



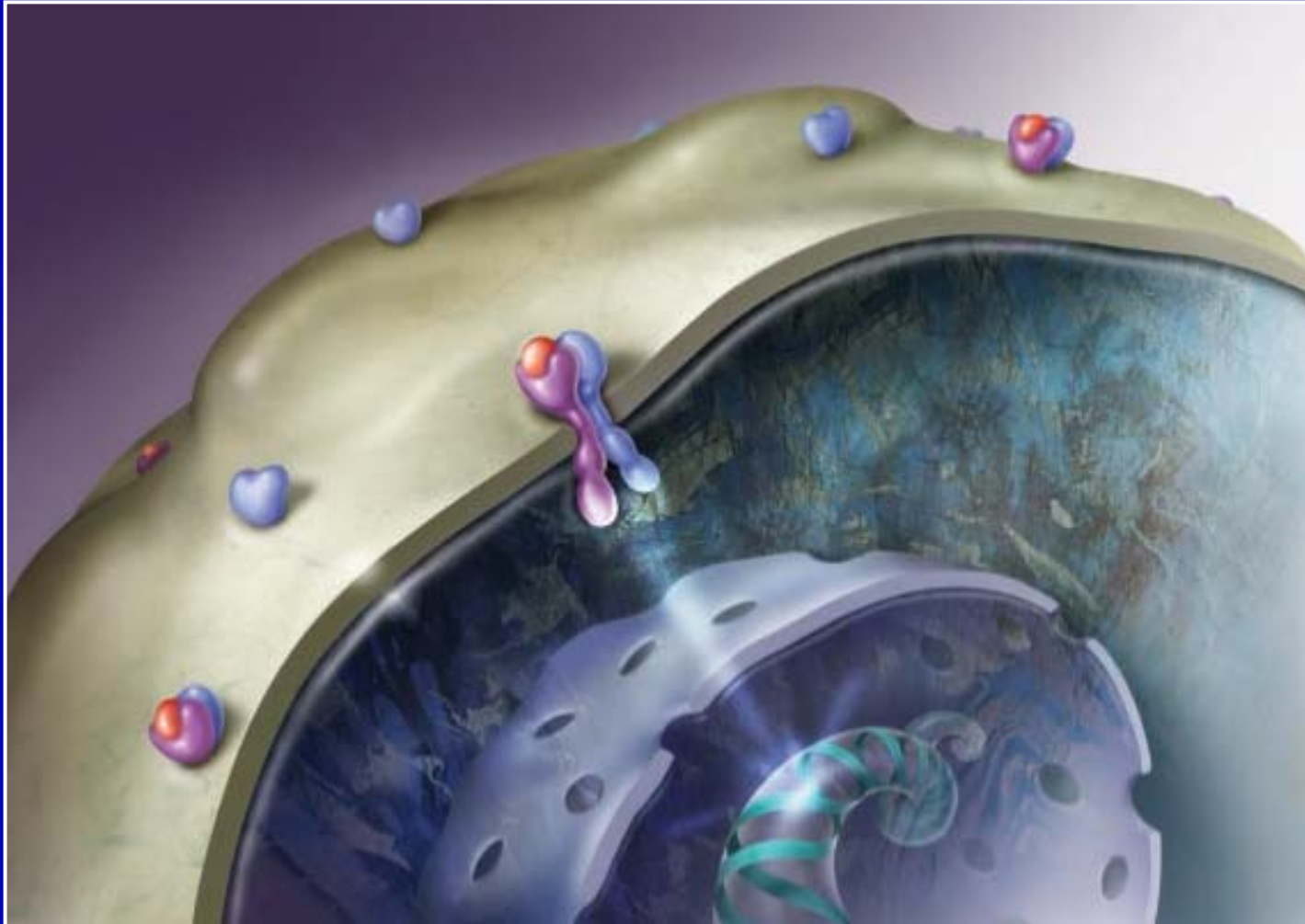
HER2 = human epidermal growth factor receptor-2

# HER2 gene amplification



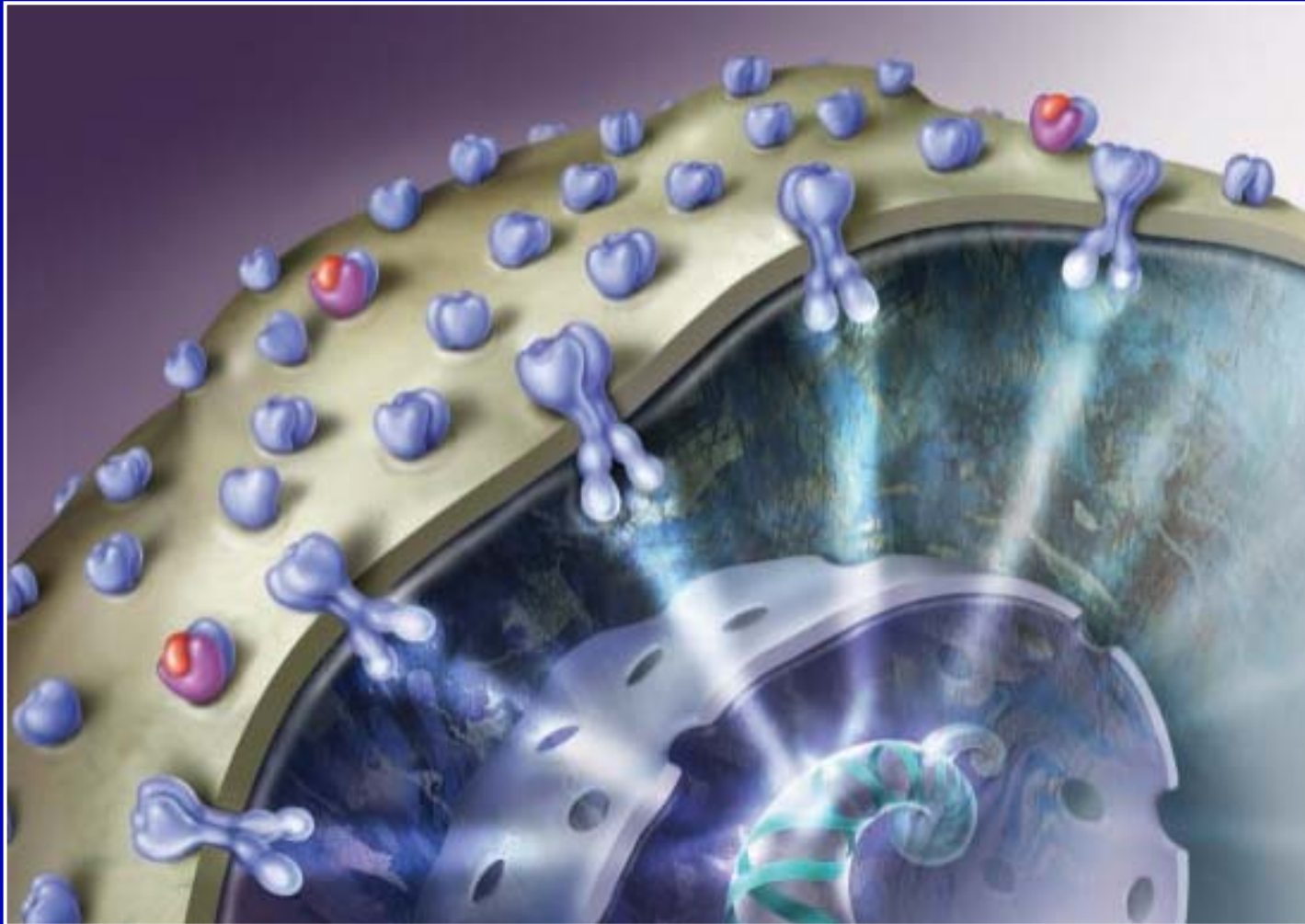
# Normal HER2 expression

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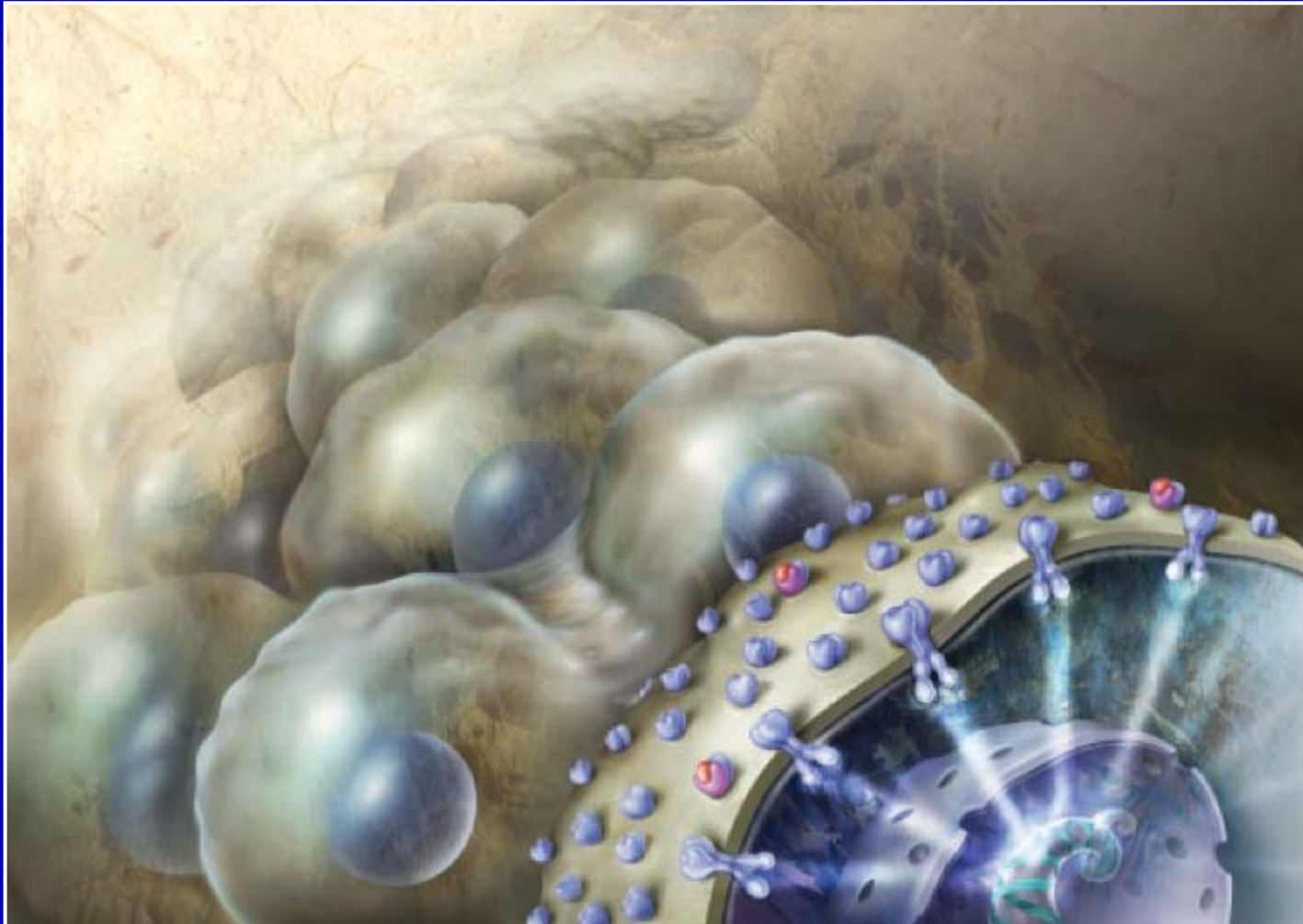
# HER2 amplification leads to HER2 overexpression

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# HER2 overexpression leads to tumour proliferation

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**Why is HER2-positive status  
important?**

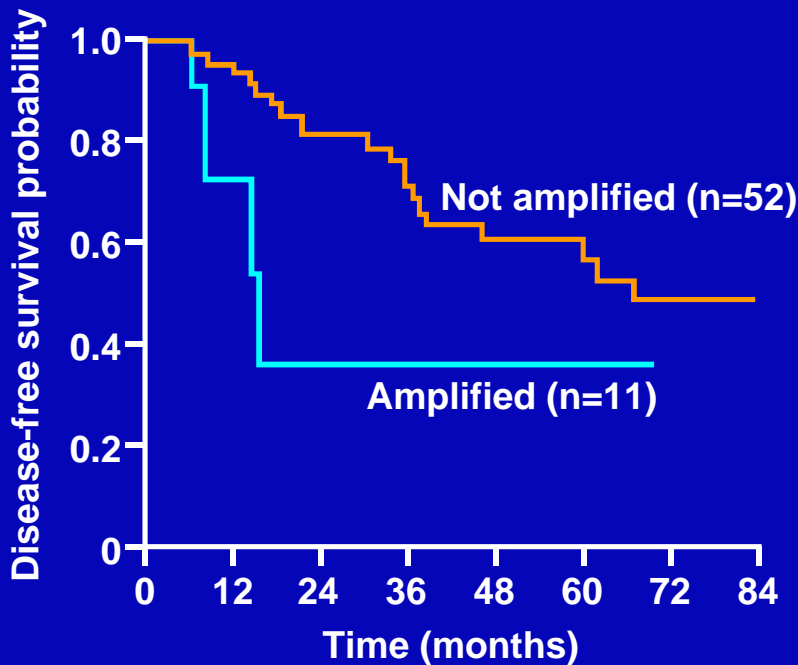
# HER2 positivity indicates a poor prognosis

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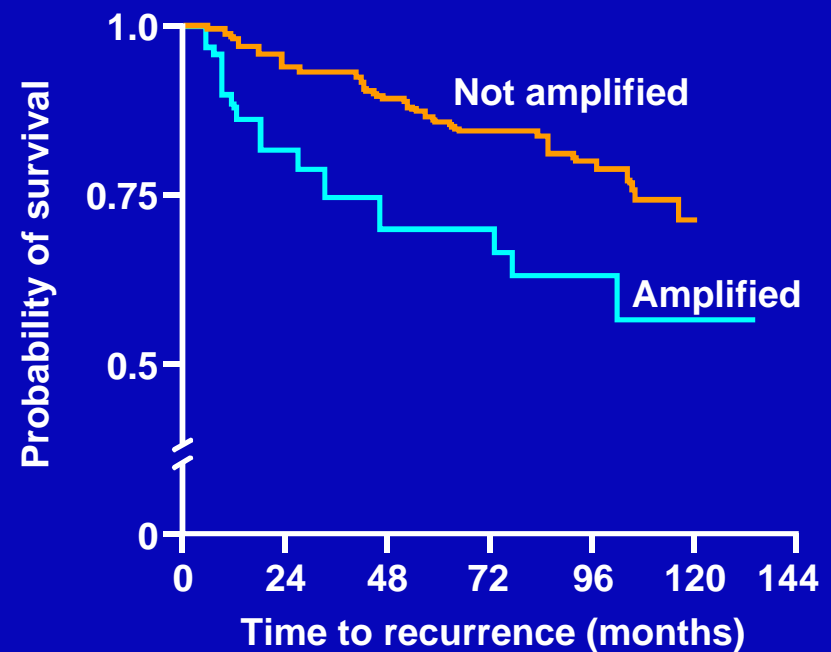
- Poorer outcome, especially in node-positive patients

# HER2 prognostic value

Slamon et al. Kaplan-Meier curve for time to relapse (disease-free survival) in **node-positive** breast cancer patients



Press et al. Kaplan-Meier curve for disease-free survival in **node-negative** breast cancer patients



Slamon DJ, et al. Science 1987;235:177-82  
Press MF, et al. J Clin Oncol 1997;15:2894-904

# HER2 as a predictive factor

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- **HER2 overexpression in breast tumours is required for response to Herceptin**
- **Predicted potential value to some therapeutic response**

# **When and how to test for HER2 status**

# When to test for HER2?

## Test all samples

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### Early testing

Performed on primary tumour at the time early breast cancer is diagnosed

### Testing at recurrence

Performed on either primary tumour or biopsy metastatic site at relapse

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# IDENTIFICATION

# Methods for detection of HER2 alterations

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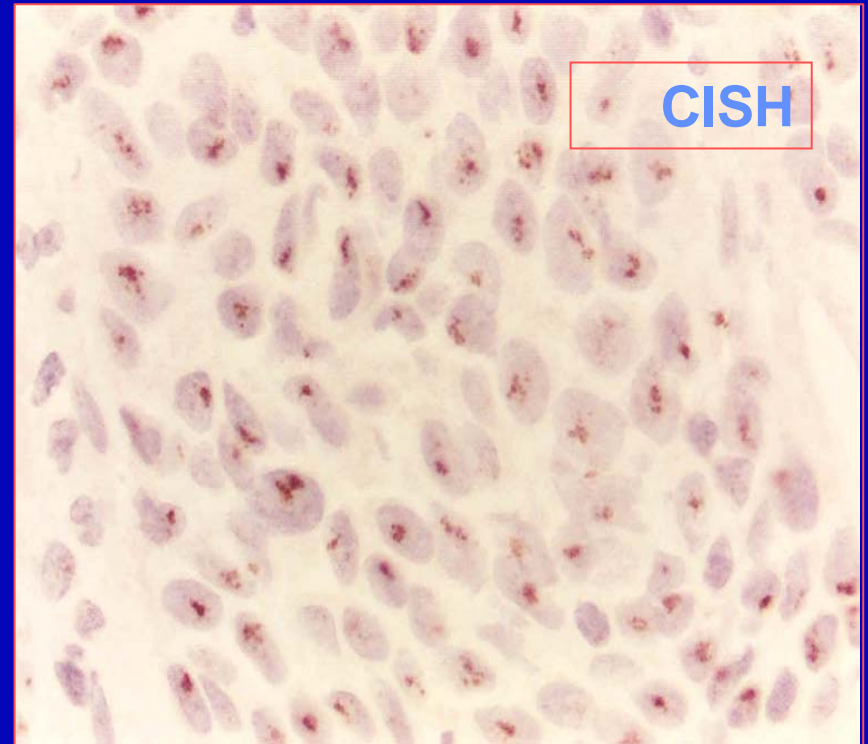
- **No morphological methods → broyats tumor**
  - Southern blot
  - PCR quantitative
  - Northern blot
  - RT-PCR quantitative
  - Western blot
  - EIA,ELISA
- **-Morphological methods → tissue preparation**
  - FISH
  - CISH
  - Immunohistochemistry



# The morphological methods are recommended

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-control cell types that show the signal

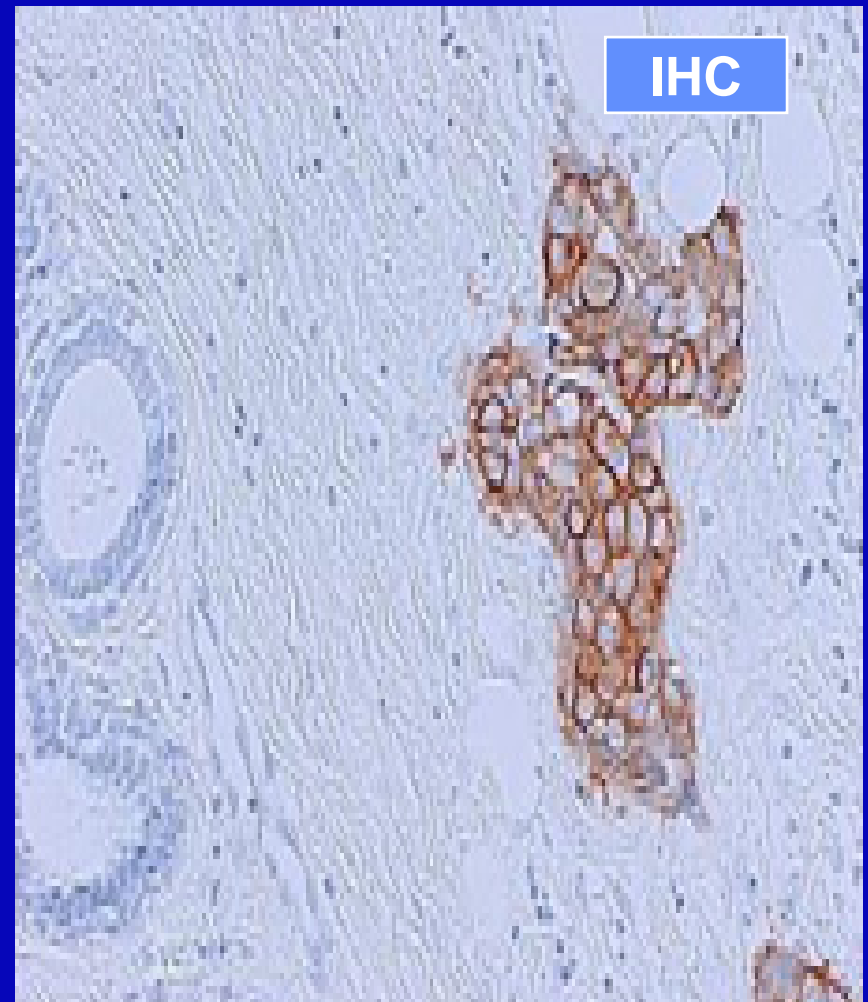


# The morphological methods are recommended

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-To control the quality of the technical:

Witness internal negative



# The morphological methods are recommended

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- IHC is recognized for determining the status HER2
- FISH, CISH: used in doubtful cases for amplification of HER2 gene

# **The importance of accurate testing**

# Importance of accurate testing

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- Poorer prognosis if HER2 positive
- Herceptin improves survival if HER2 positive, but not if HER2 negative
  - **false-negative assessment:** denies patients life-extending treatment
  - **false-positive assessment:** patients will not benefit from Herceptin therapy

# Pros and cons of HER2 testing methods

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- IHC

- pro: well established, highest predictive value
- con: result is antibody and observer dependent

- FISH CISH

- pro: quantifies number of HER2 signals
- con: expensive, interobserver discordance not well known

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**Evaluation of oestrogen and  
progesterone receptor status in  
HER positive breast carcinoma and  
correlation with outcome**

# Méthods

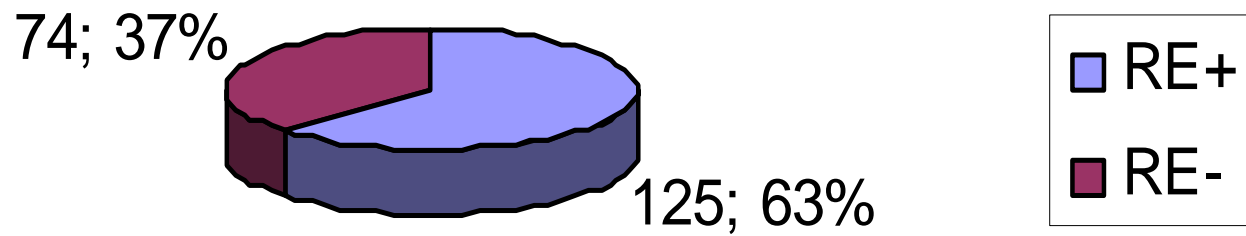
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- 200 cases of breast carcinoma during a period of 02 years
- All these cases were evaluated using IHC for ER,PR and HER2



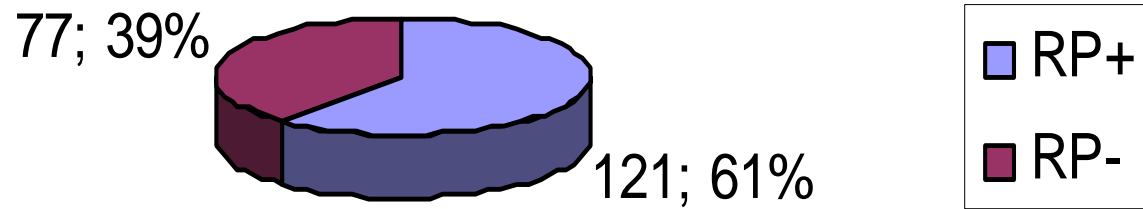
# Résultats

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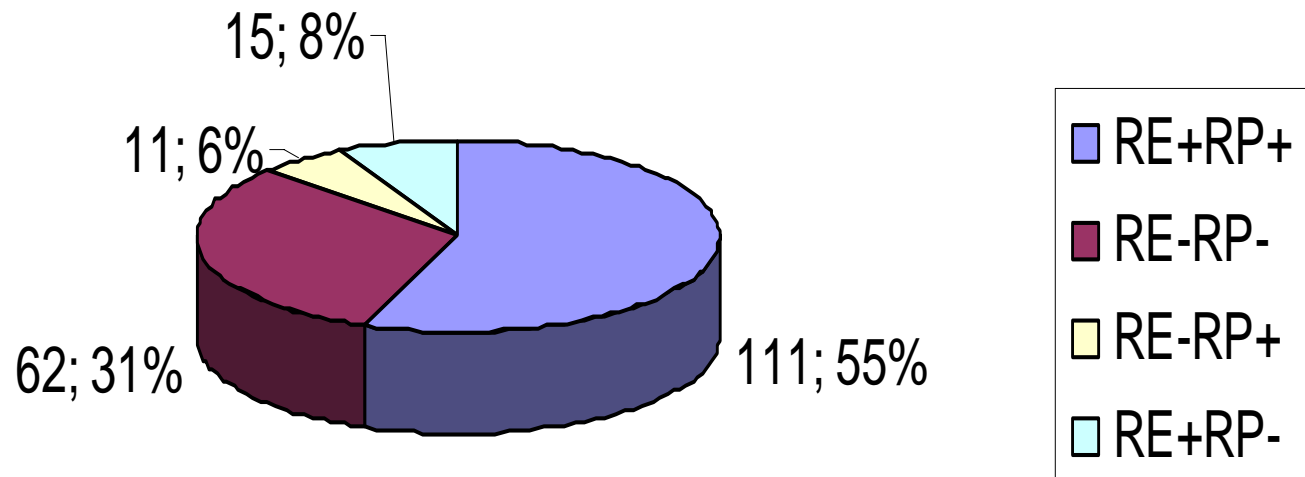


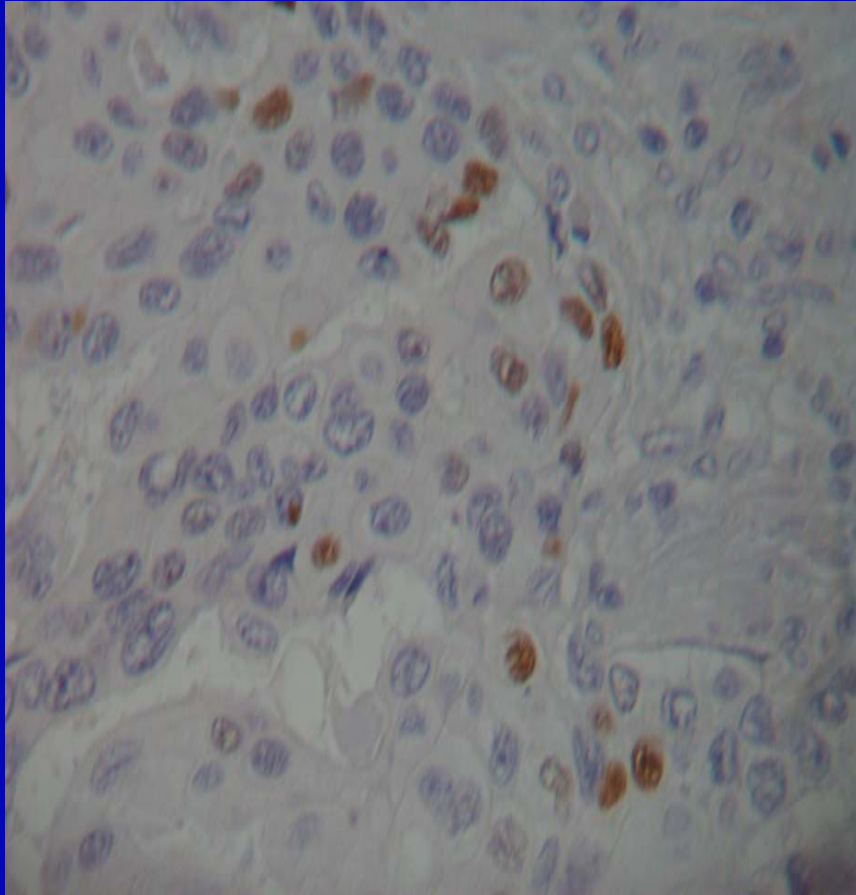
# Résultats

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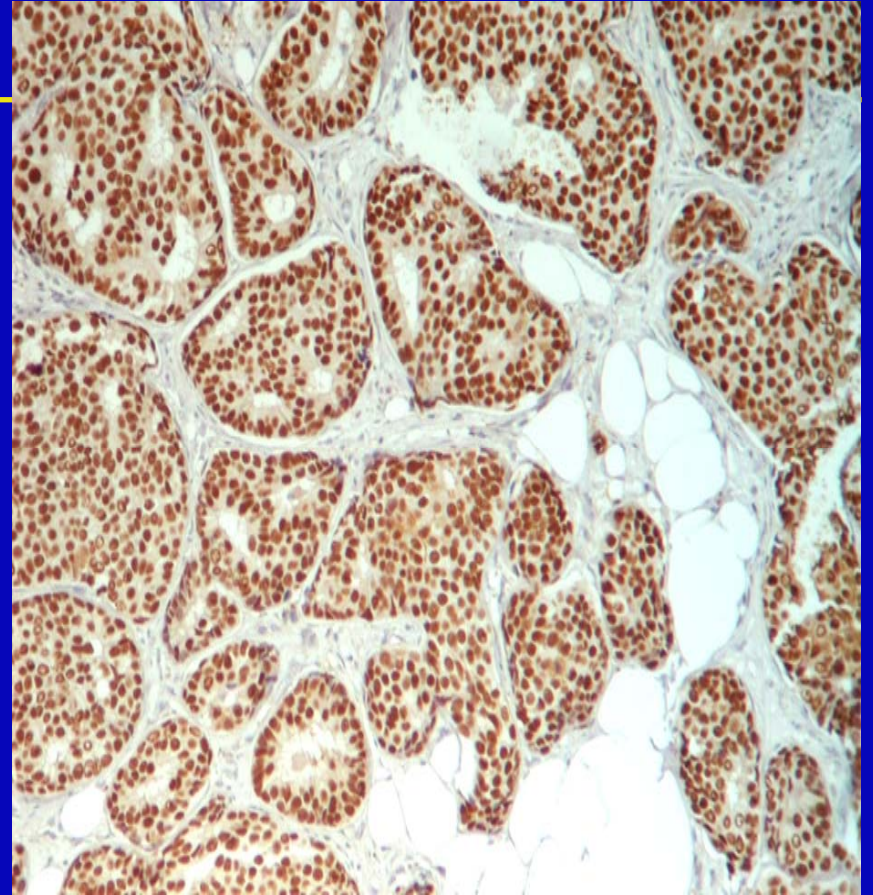


# Résultats



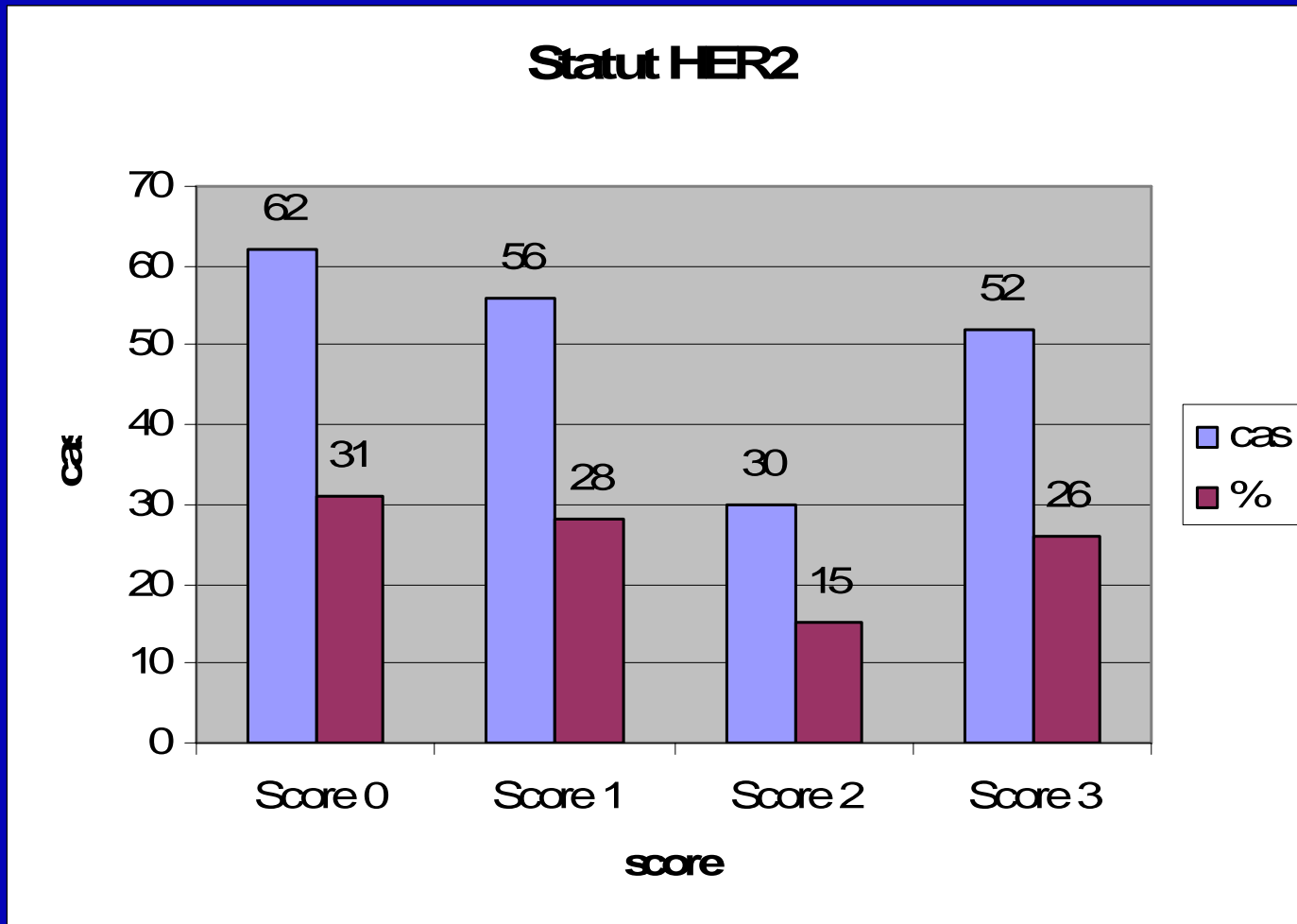


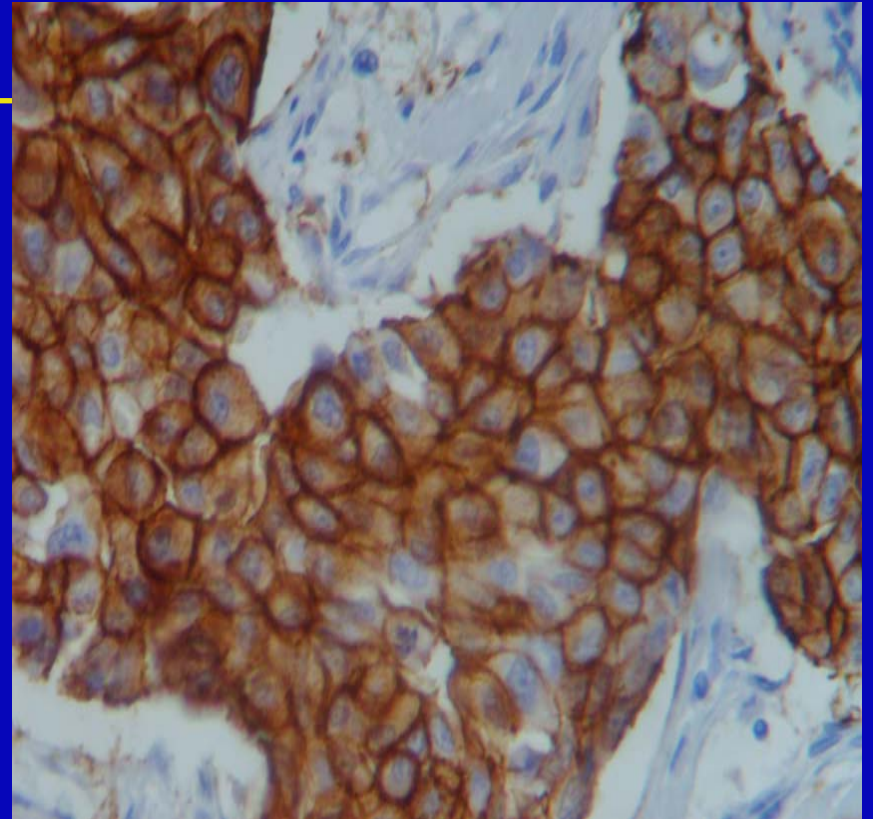
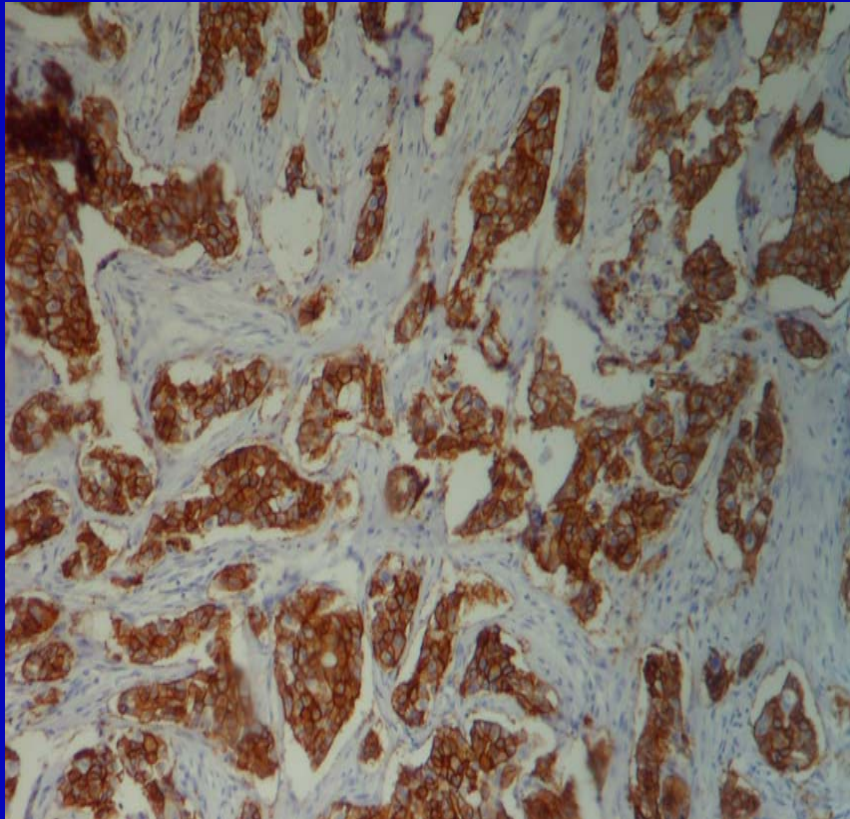
**HR low positivity**



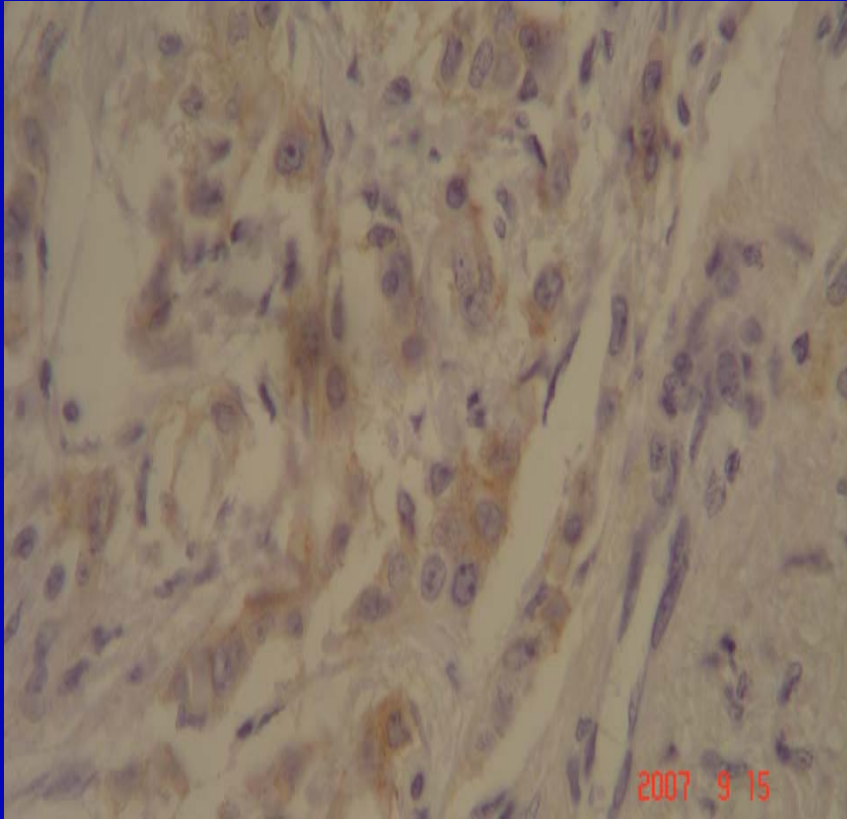
**HR strong positivity**

# Résultats

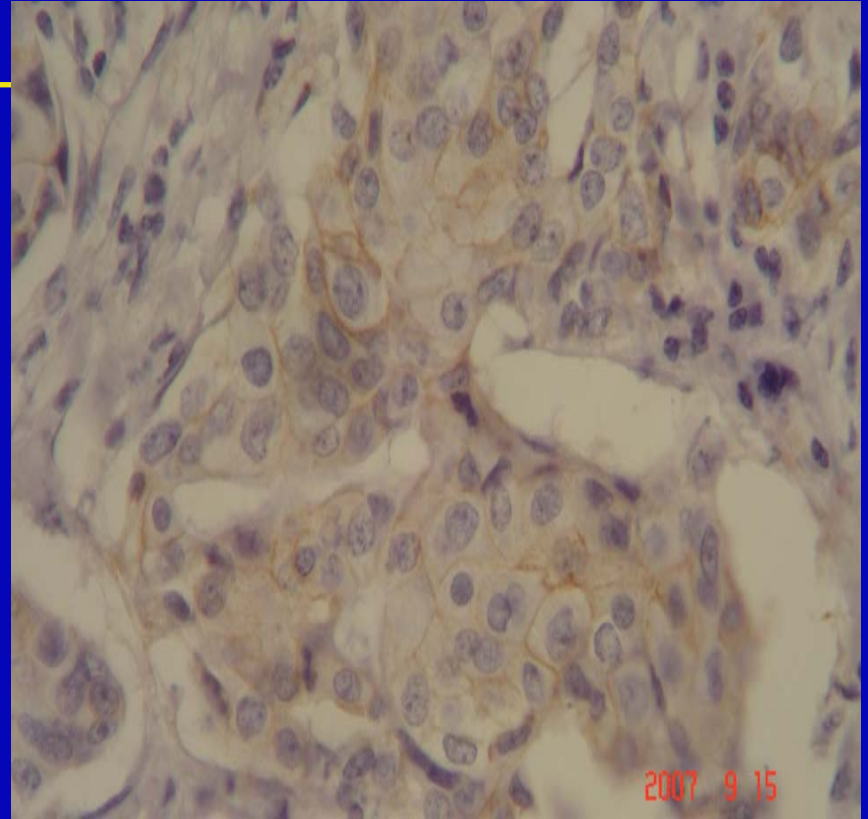




**'3+' (positive)**

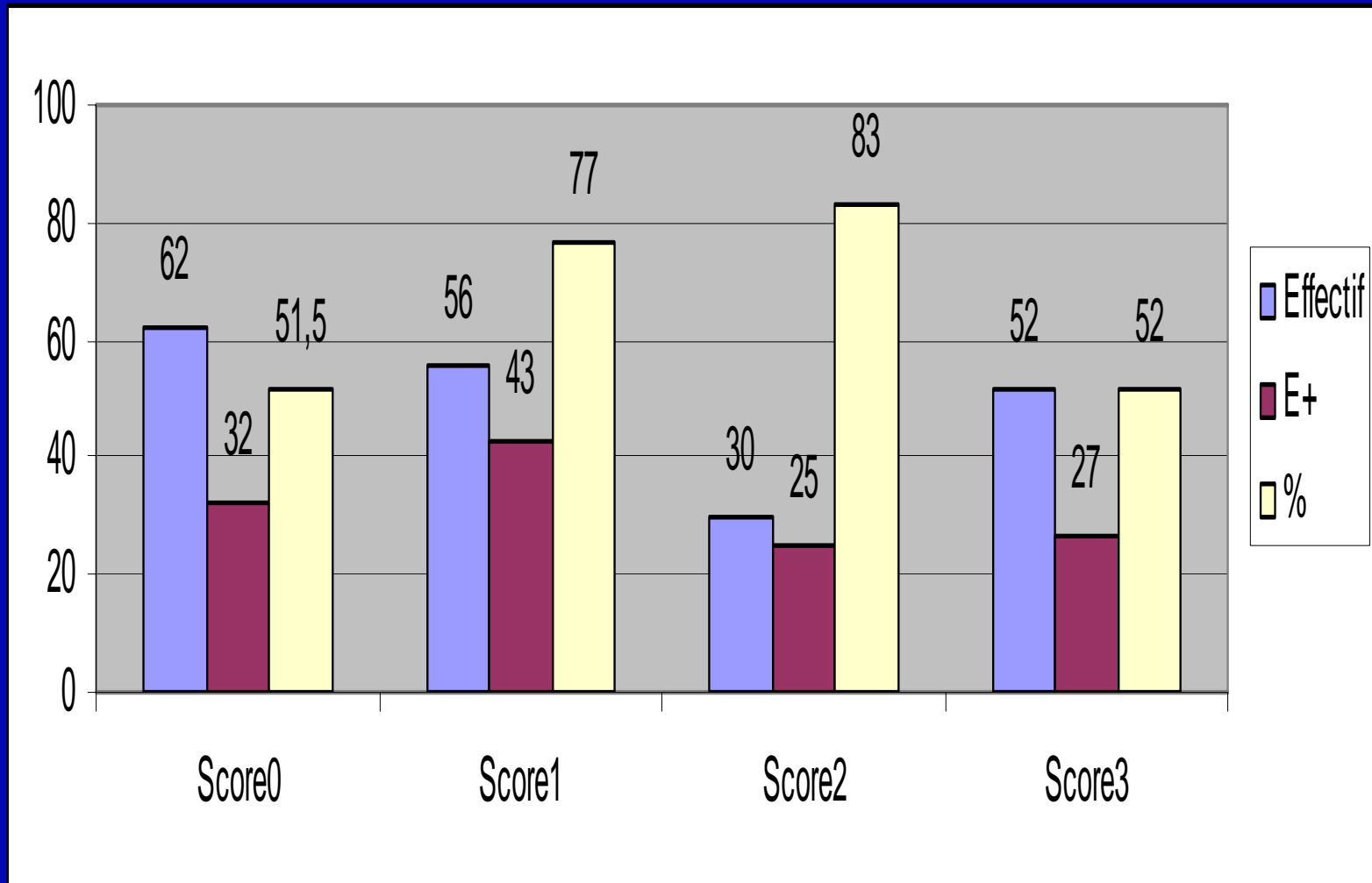


**1+' (negative)**



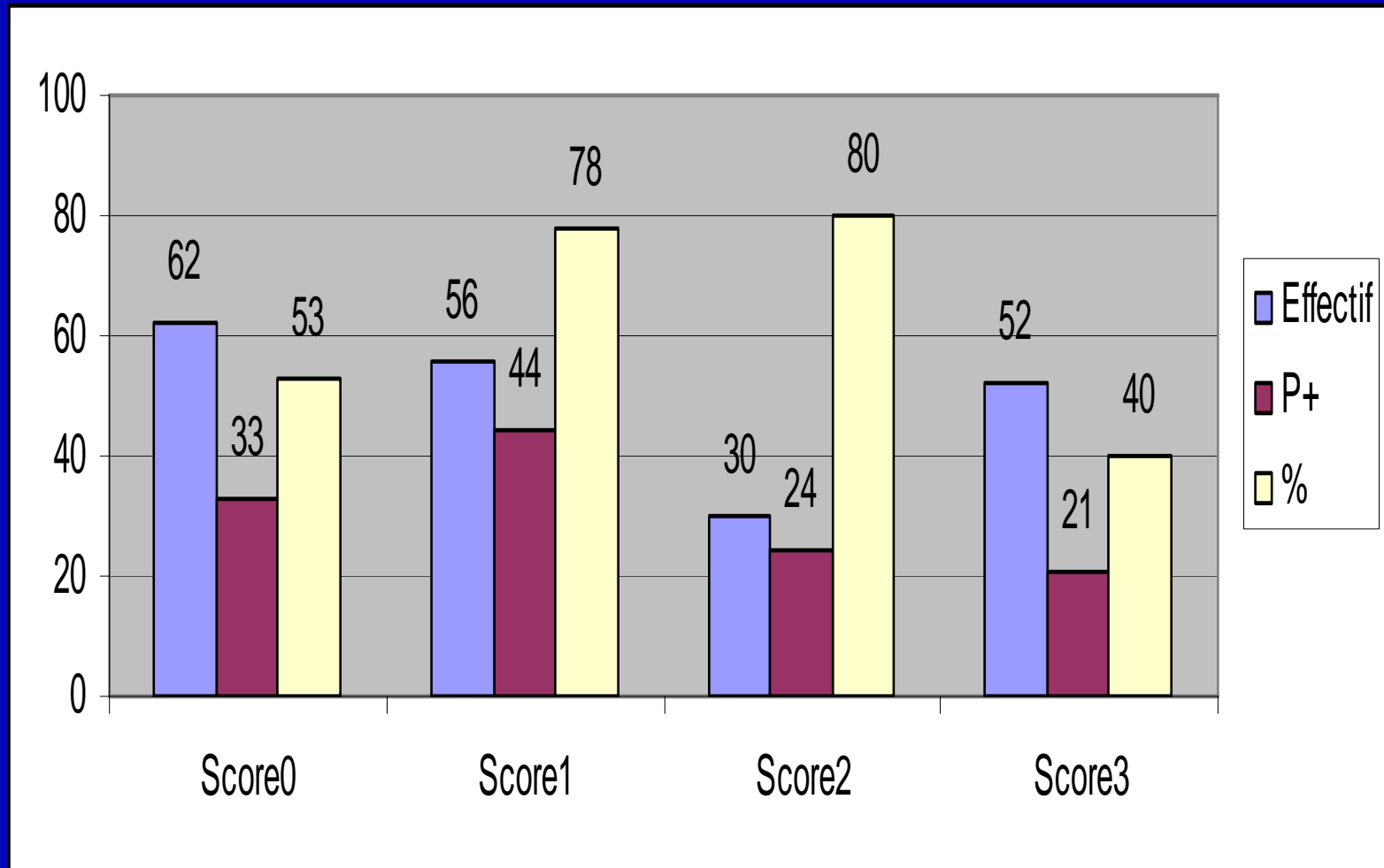
**'2+' (equivocal)**

# Résultats:ER/HER2

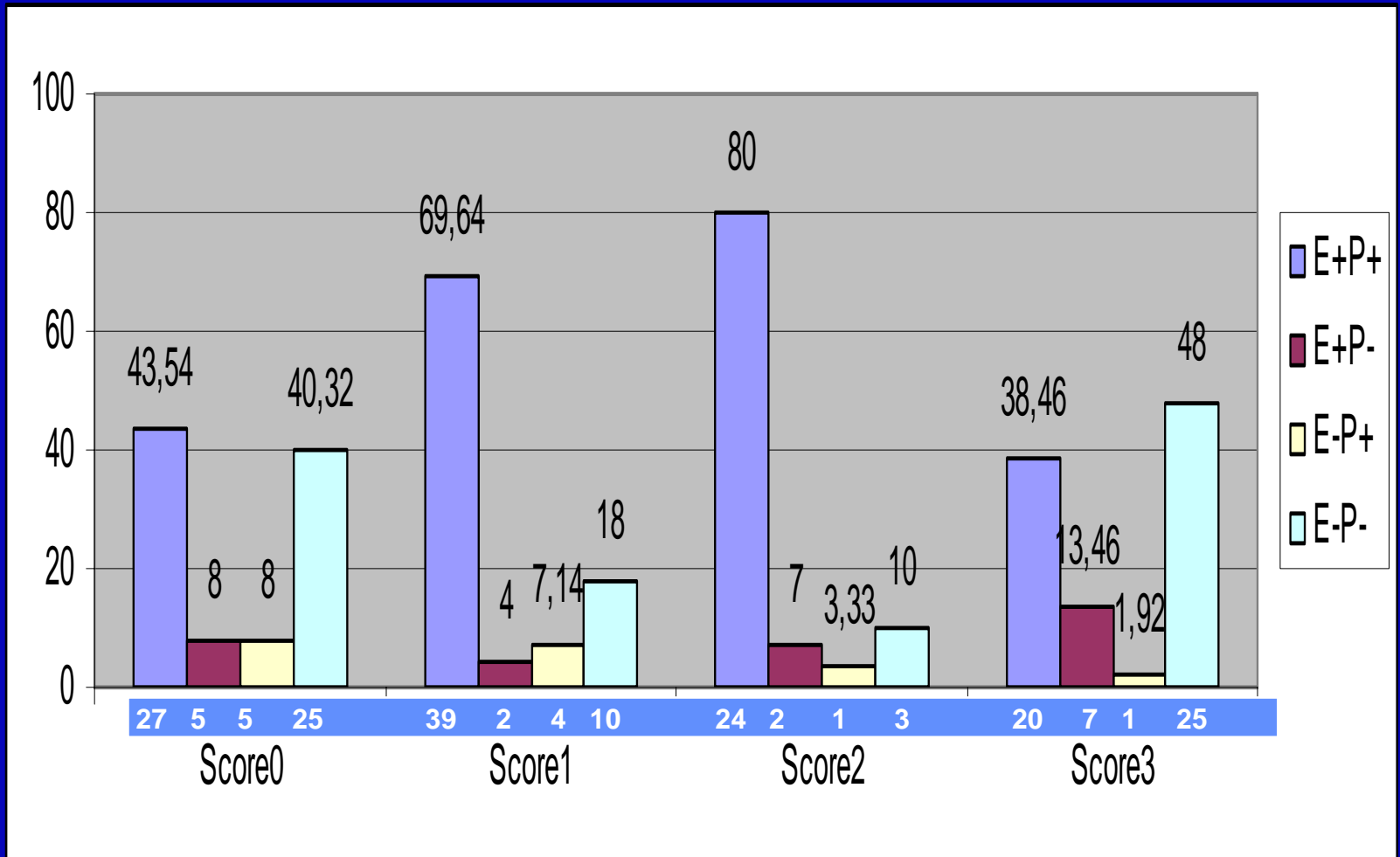




# Résultats:PR/HER2



# Résultats:RH/HER2



# Discussion

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- **HER2 amplification occurs in 15-30% of breast carcinomas**
- **HER2 is found in 50% of CLC**
- **>90% in Paget's disease**
- **For a technique well-balanced HER2 IHC 2 + score: 10à20%**
- **Presence of at least 60% of marked cells is associated with amplification whatever the intensity of marking (GEFPICS)**

# Discussion

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- **Approximately 50 % of HER2 breast cancers are HR+**
- **Patients « co-positive » often have metastatic cancer and poor response to hormone therapy .**

# Discussion

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- For RP: contradictory results
- Among the HER + only 8 to 24% are PR + for some authors
- Yang found 48% of RP associated with her in his series of 245 carcinomas which is in line with our results

# Discussion

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- **Currently it has been demonstrated that the RP is genetically heterozygous**
- **The absence of PR may not simply reflect a lack of ER activity but rather may reflect hyperactive cross-talk between ER and HER2**
- **His loss is correlated with overexpression of HER2 and contributes to the strength of Tamoxifen**

# Discussion

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- A randomized study shows that women with RE + Premenopause respond to hormone therapy regardless of HER2
- The study confirms an age-related inverse relationship between HER2 and PR in woman age >45 years but not in woman age < 45 years

# Conclusion

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- **amplification and / or overexpression of HER2 is certainly a target therapeutic value and seems important prognostic factor.**
- **Its role in the prediction of responses to different treatments require confirmation.**



# Conclusion

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- Despite the difficulties of standardization, the IHC should be the standard method for the identification of an overexpression of HER2
- For doubtful cases → redoing the technical → FISH or CISH if doubts persist

# Conclusion

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- The laboratories have to determine the tumor status and HER2 HR must participate in internal quality controls or external
- HR are inversely proportional to antigen neu expression.
- Relationship remains unexplained, the results vary between authors and remain promising