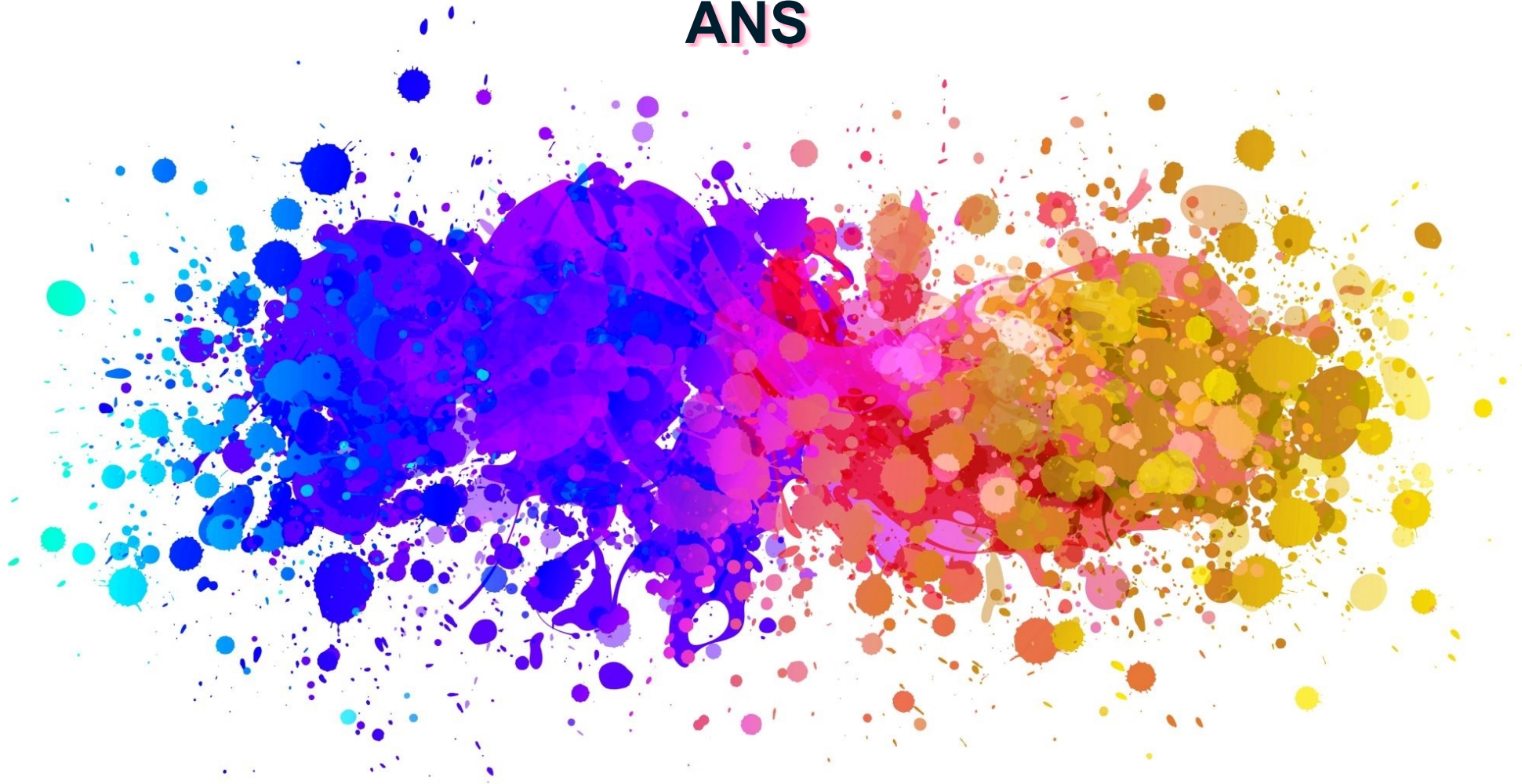


# **PARTICULARITÉS DU CANCER DU SEIN INVASIF EN FRANCE CHEZ LA FEMME DE MOINS DE 40 ANS ET DE PLUS DE 70 ANS**



Dr BAILLEUX Caroline (Nice)  
SFSPM 2022

# ***LIENS D'INTÉRÊT***

Novartis, Lilly, Pfizer

AstraZeneca, Daiichi-Sankyo,  
Seagen

Roche, Viartis, Gilead

# BREAST CANCER IS THE MOST COMMON CANCER IN U.S. WOMEN AGES 15-39

## TOP 5 INVASIVE CANCERS DIAGNOSED IN YOUNG WOMEN

BREAST

38%

MELANOMA

20%

UTERINE CERVIX 12%

LEUKEMIA 10%

NON-HODGKINS LYMPHOMA 7%

BASED ON PROBABILITY OF DEVELOPING BREAST CANCER  
AMERICAN CANCER SOCIETY,  
SURVEILLANCE RESEARCH, 2013

 **35**  
MORE THAN  
YOUNG WOMEN ARE DIAGNOSED  
WITH BREAST CANCER  
EVERY DAY

AMERICAN CANCER SOCIETY, CANCER FACTS & FIGURES 2013-2014

1 American Cancer Society, Cancer Facts and Figures 2013-2014

2 12.5% of total breast cancer under 45. ACS, 2013-2014

Données INCA 2012:  
20% des cancers du sein  $\geq 75$  ans



# Facteurs de risque

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- Génétiques : BRCA, p53, PTEN, Rôle de IGF-I, IGBP-3

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  - plus de 10 ans : RR=2,2
  - >10 ans et débutée avant 18 ans : RR=3,1

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- Grossesse :
  - Rôle protecteur de l'allaitement > 3 mois
  - IVG : RR=1,5
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  - IVG<18 ans : RR=2,5
- Habitus : pas d'effet de l'alcool, du tabac, de la caféine...

# **Caractéristiques des tumeurs selon l'âge**

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# Caractéristiques des tumeurs selon l'âge

|                        | EIO <sup>1</sup> (non méta) |       | MDACC <sup>2</sup> (non méta) |
|------------------------|-----------------------------|-------|-------------------------------|
|                        | ≤ 35                        | 36-50 | ≤ 35                          |
| <b>Patientes</b>       | 101                         | 740   | 452                           |
| <b>RO +</b>            | 57%                         | 82%   | 52%                           |
| <b>RP +</b>            | 51%                         | 77%   | 47%                           |
| <b>Ki 67 &gt; 20%</b>  | 62%                         | 50%   | -                             |
| <b>Grade 3</b>         | 48%                         | 32%   | 69%                           |
| <b>HER2 3+</b>         | 20%                         | 15%   | 34%                           |
| <b>T &gt; 3 cm</b>     | 6%                          | 3%    | -                             |
| <b>Méta hépatiques</b> | -                           | -     | -                             |

1. Colleoni et al, Ann Oncol 2006 2. Gonzales-Angulo AM, Cancer 2006

# Caractéristiques des tumeurs selon l'âge (non méta)

**Table 1**

Characteristics of primary tumor and adjuvant treatment: overall and across age groups(\*%/available data; \*\*%/all patients).

|                          | All<br>N = 14403 | Age at MBC      |         |                         |         |                       |         | P value between age groups |
|--------------------------|------------------|-----------------|---------|-------------------------|---------|-----------------------|---------|----------------------------|
|                          |                  | <40<br>N = 1077 |         | 40–60 years<br>N = 6436 |         | >60 years<br>N = 6890 |         |                            |
|                          |                  | N               | %       | N                       | %       | N                     | %       |                            |
| <b>Tumor size (cT)</b>   |                  |                 |         |                         |         |                       |         | <b>&lt;0.0001</b>          |
| T0                       | 164              | 4               | 0.7%*   | 75                      | 2.5%*   | 85                    | 2.8%*   |                            |
| T1                       | 1297             | 75              | 13.4%*  | 548                     | 17.9%*  | 674                   | 22.4%*  |                            |
| T2                       | 2389             | 210             | 37.6%*  | 1119                    | 36.6%*  | 1060                  | 35.3%*  |                            |
| T3                       | 1192             | 156             | 28.0%*  | 617                     | 20.2%*  | 419                   | 13.9%*  |                            |
| T4 global                | 1579             | 113             | 20.3%*  | 698                     | 22.8%*  | 768                   | 25.5%*  |                            |
| Not available            | 7782             | 519             | 48.2%** | 3379                    | 52.5%** | 3884                  | 56.4%** |                            |
| <b>Nodal status (cN)</b> |                  |                 |         |                         |         |                       |         | <b>&lt;0.0001</b>          |
| N0                       | 2740             | 183             | 34.7%*  | 1201                    | 41.5%*  | 1356                  | 48.6%*  |                            |
| N1                       | 2513             | 242             | 45.9%*  | 1235                    | 42.6%*  | 1036                  | 37.1%*  |                            |
| N2                       | 575              | 63              | 12.0%*  | 273                     | 9.4%*   | 239                   | 8.6%*   |                            |
| N3                       | 386              | 39              | 7.4%*   | 188                     | 6.5%*   | 159                   | 5.7%*   |                            |
| Not available            | 8189             | 550             | 51.1%** | 3539                    | 55.0%** | 4100                  | 59.5%** |                            |
| <b>Grade</b>             |                  |                 |         |                         |         |                       |         | <b>&lt;0.0001</b>          |
| I                        | 915              | 26              | 2.6%*   | 346                     | 5.9%*   | 543                   | 8.8%*   |                            |
| II                       | 6247             | 352             | 35.1%*  | 2711                    | 45.9%*  | 3184                  | 51.3%*  |                            |
| III                      | 5947             | 624             | 62.3%*  | 2847                    | 48.2%*  | 2476                  | 39.9%*  |                            |
| Not available            | 1294             | 75              | 7.0%**  | 532                     | 8.3%**  | 687                   | 10.0%** |                            |
| <b>Histological type</b> |                  |                 |         |                         |         |                       |         | <b>&lt;0.0001</b>          |
| Ductal                   | 11317            | 973             | 97.0%*  | 5281                    | 89.3%*  | 5063                  | 80.8%*  |                            |
| Lobular                  | 1868             | 30              | 3.0%*   | 636                     | 10.7%*  | 1202                  | 19.2%*  |                            |
| Other or Not available   | 1218             | 74              | 6.9%**  | 519                     | 8.0%**  | 625                   | 9.0%**  |                            |

# Caractéristiques des tumeurs selon l'âge

|                        | EIO <sup>1</sup> (non méta) |       | MDACC <sup>2</sup> (non méta) | ESME <sup>3</sup> (Méta) |      |
|------------------------|-----------------------------|-------|-------------------------------|--------------------------|------|
|                        | ≤ 35                        | 36-50 | ≤ 35                          | < 40                     | > 60 |
| <b>Patientes</b>       | 101                         | 740   | 452                           | 1077                     | 6890 |
| <b>RO +</b>            | 57%                         | 82%   | 52%                           | 48%                      | 72%  |
| <b>RP +</b>            | 51%                         | 77%   | 47%                           | -                        | -    |
| <b>Ki 67 &gt; 20%</b>  | 62%                         | 50%   | -                             | -                        | -    |
| <b>Grade 3</b>         | 48%                         | 32%   | 69%                           | 62%                      | 40%  |
| <b>HER2 3+</b>         | 20%                         | 15%   | 34%                           | 26%                      | 16%  |
| <b>T &gt; 3 cm</b>     | 6%                          | 3%    | -                             | 48%                      | 43%  |
| <b>Méta hépatiques</b> | -                           | -     | -                             | 36%                      | 15%  |

1. Colleoni et al, Ann Oncol 2006

2. Gonzales-Angulo AM, Cancer 2006

3. Franck S et al, Breast 2020

# Caractéristiques des tumeurs selon l'âge (méta)

**Table 2**

Metastatic breast cancer characteristics according to age groups.

|  | All  |       | Age at MBC |       |               |       |           |       | <i>P value between age groups</i> |         |
|--|------|-------|------------|-------|---------------|-------|-----------|-------|-----------------------------------|---------|
|  |      |       | <40 years  |       | [40–60] years |       | >60 years |       |                                   |         |
|  | N    | %     | N          | %     | N             | %     | N         | %     |                                   |         |
| <b>Time to first metastasis</b>          |      |       |            |       |               |       |           |       |                                   | <0.0001 |
| <i>De novo (&lt; 3 months)</i>           | 4058 | 28.2% | 339        | 31.5% | 1849          | 28.7% | 1870      | 27.1% |                                   |         |
| <i>[3–24[ months</i>                     | 2284 | 15.9% | 308        | 28.6% | 1114          | 17.3% | 862       | 12.5% |                                   |         |
| <i>&gt;= 24 months</i>                   | 8035 | 55.8% | 429        | 39.8% | 3461          | 53.8% | 4145      | 60.2% |                                   |         |
| <i>NA</i>                                | 26   | 0.2%  | 1          | 0.1%  | 12            | 0.2%  | 13        | 0.2%  |                                   |         |
| <b>Number of metastatic sites</b>        |      |       |            |       |               |       |           |       |                                   | 0.02    |
| <i>One site</i>                          | 7976 | 55.4% | 572        | 53.1% | 3493          | 54.3% | 3911      | 56.8% |                                   |         |
| <i>Two sites</i>                         | 3473 | 24.1% | 267        | 24.8% | 1586          | 24.6% | 1620      | 23.5% |                                   |         |
| <i>Three or more sites</i>               | 2954 | 20.5% | 238        | 22.1% | 1357          | 21.1% | 1359      | 19.7% |                                   |         |
| <b>Type of metastasis</b>                |      |       |            |       |               |       |           |       |                                   | <0.0001 |
| <i>Bone only</i>                         | 8145 | 65.3% | 562        | 52.2% | 3587          | 55.7% | 3996      | 58.0% |                                   |         |
| <i>Visceral</i>                          | 4584 | 15.6% | 391        | 36.3% | 2140          | 33.3% | 2053      | 29.8% |                                   |         |
| <i>Other (neither visceral nor bone)</i> | 1674 | 19.1% | 124        | 11.5% | 709           | 11.0% | 841       | 12.2% |                                   |         |

# **Sous-types histologiques selon l'âge**

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# Sous-types histologiques selon l'âge

**Table 1**

Characteristics of primary tumor and adjuvant treatment: overall and across age groups(\*%/available data; \*\*%/all patients).

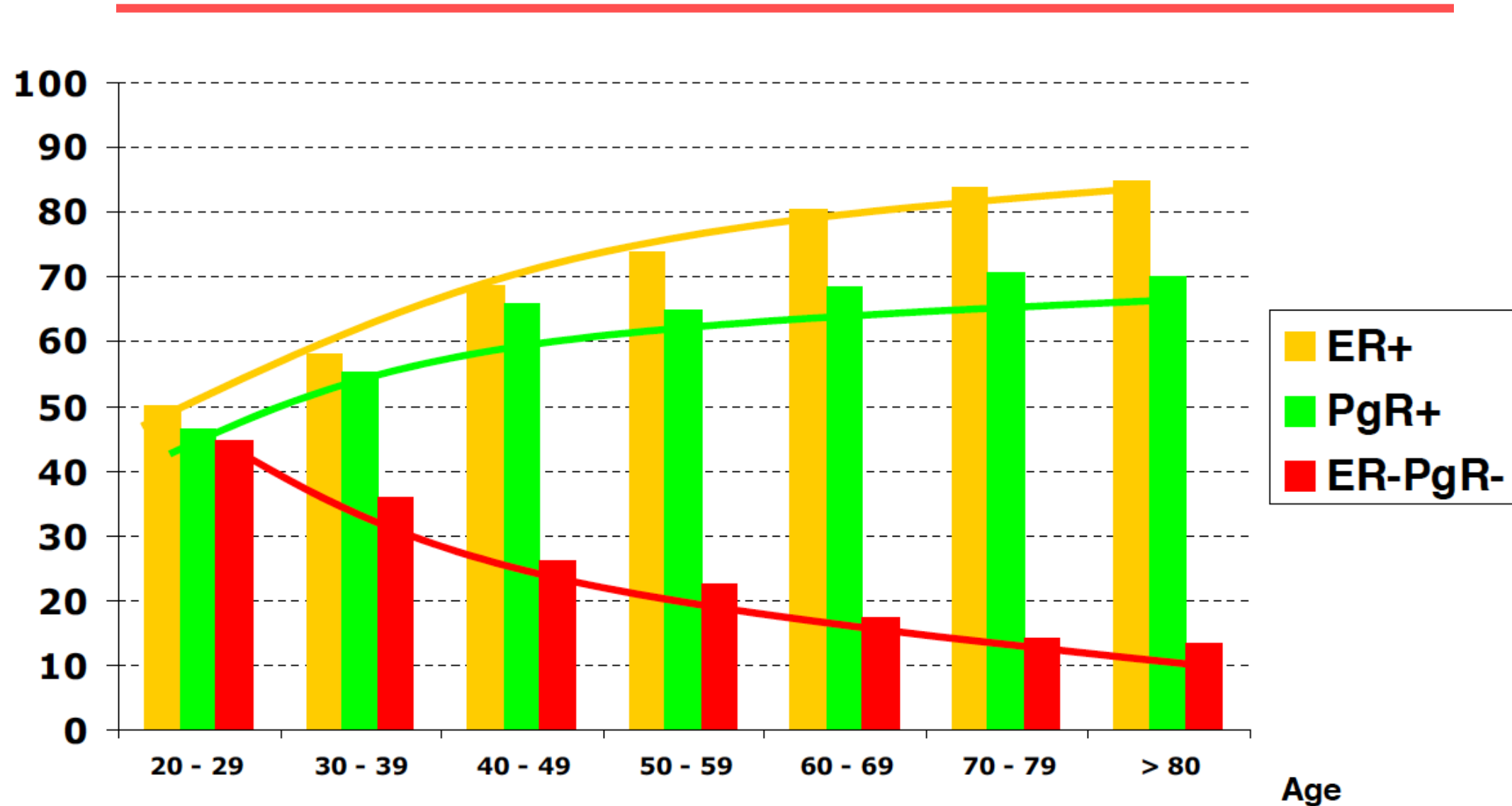
|                 | All<br>N = 14403 | Age at MBC      |        |                         |        |                       |         | P value between age groups |
|-----------------|------------------|-----------------|--------|-------------------------|--------|-----------------------|---------|----------------------------|
|                 |                  | <40<br>N = 1077 |        | 40–60 years<br>N = 6436 |        | >60 years<br>N = 6890 |         |                            |
|                 |                  | N               | %      | N                       | %      | N                     | %       |                            |
| <b>Subtypes</b> |                  |                 |        |                         |        |                       |         | <b>&lt;0.0001</b>          |
| HoR + Her2-     | 8391             | 502             | 47.5%* | 3604                    | 60.0%* | 4285                  | 70.3%*  |                            |
| HoR-Her2-       | 2298             | 283             | 26.8%* | 1163                    | 19.4%* | 852                   | 14.0%*  |                            |
| Her2+           | 2465             | 271             | 25.7%* | 1238                    | 20.6%* | 956                   | 15.7%*  |                            |
| Not available   | 1249             | 21              | 1.9%** | 431                     | 6.7%** | 797                   | 11.6%** |                            |

**Table 2**

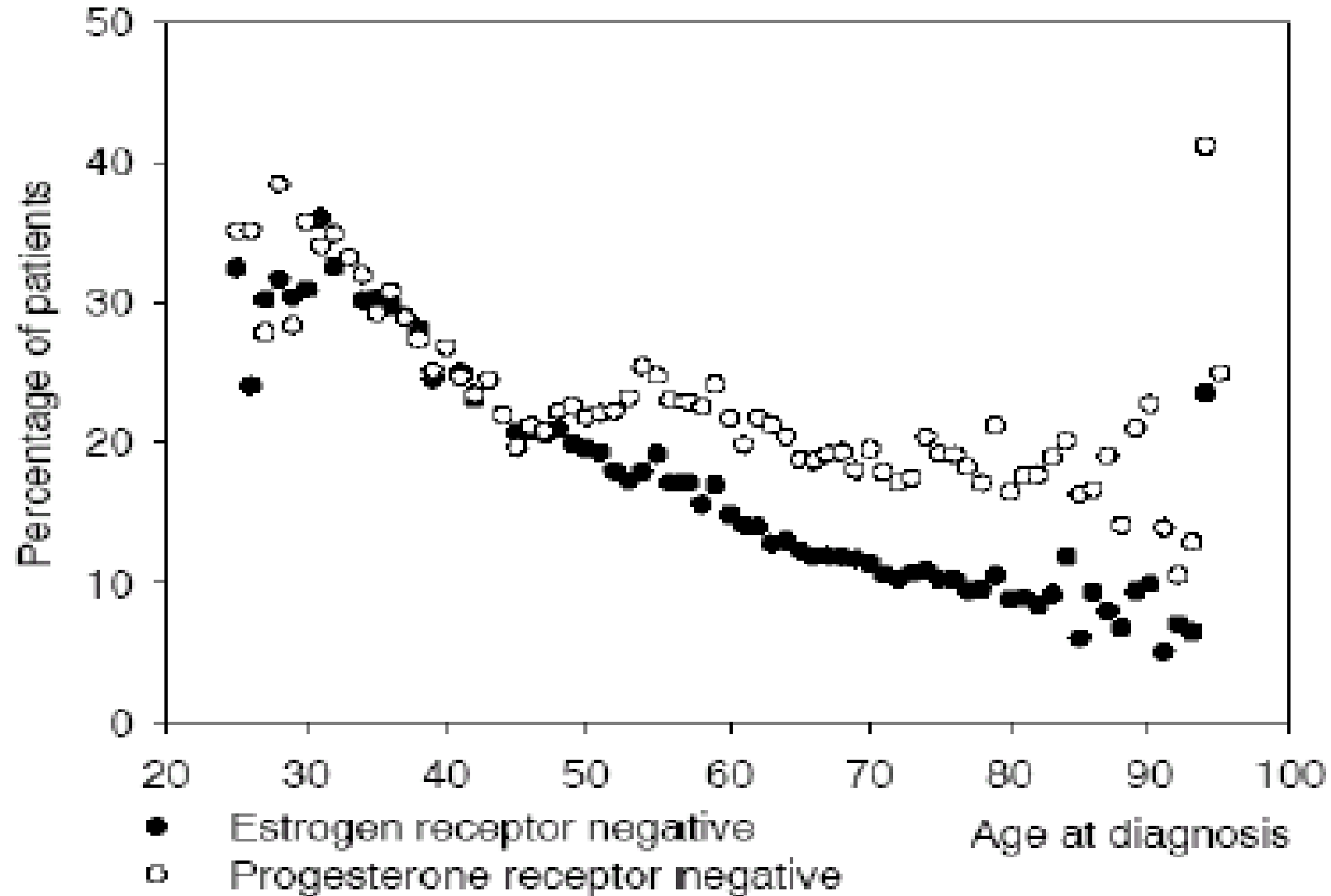
Metastatic breast cancer characteristics according to age groups.

| Tumor subtype        | All  |       | Age at MBC |       |               |       |           |       | P value between age groups |
|----------------------|------|-------|------------|-------|---------------|-------|-----------|-------|----------------------------|
|                      |      |       | <40 years  |       | [40–60] years |       | >60 years |       |                            |
|                      | N    | %     | N          | %     | N             | %     | N         | %     |                            |
| <b>Tumor subtype</b> |      |       |            |       |               |       |           |       | <b>&lt;0.0001</b>          |
| HoR + HER2-          | 9398 | 15.6% | 519        | 48.2% | 3934          | 61.1% | 4945      | 71.8% |                            |
| HoR-HER2-            | 2247 | 19.1% | 272        | 25.3% | 1138          | 17.7% | 837       | 12.1% |                            |
| HER2+                | 2758 | 65.3% | 286        | 26.6% | 1364          | 21.2% | 1108      | 16.1% |                            |

# Répartition des tumeurs selon les RH et l'âge (méta et non méta)



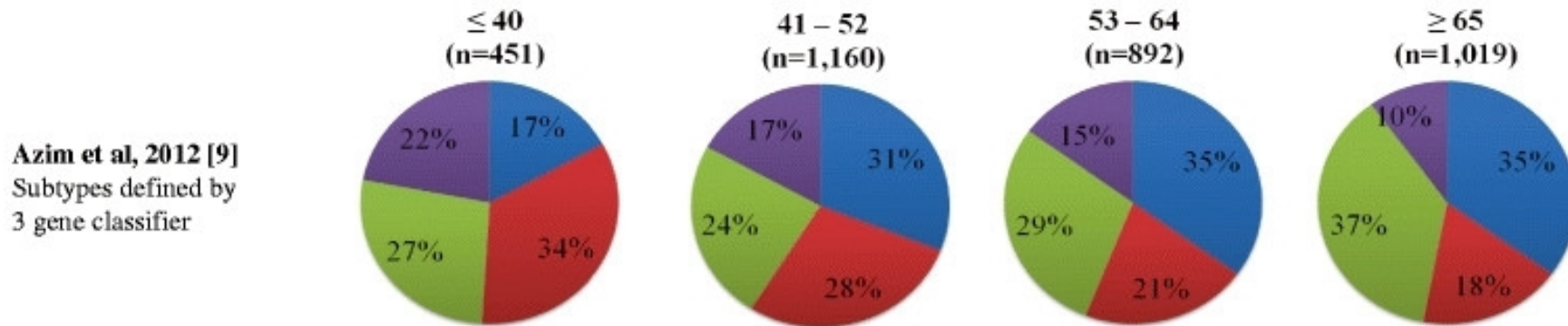
# Répartition des tumeurs T1-2 selon les RH et l'âge (non méta)



# Répartition des sous-types histologiques en fonction de l'âge

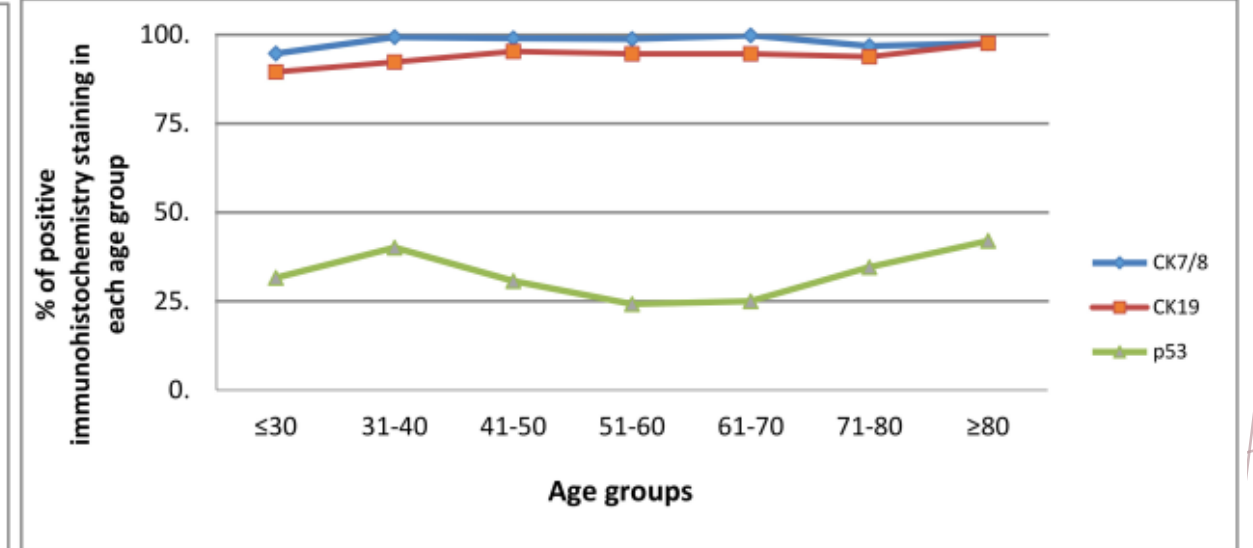
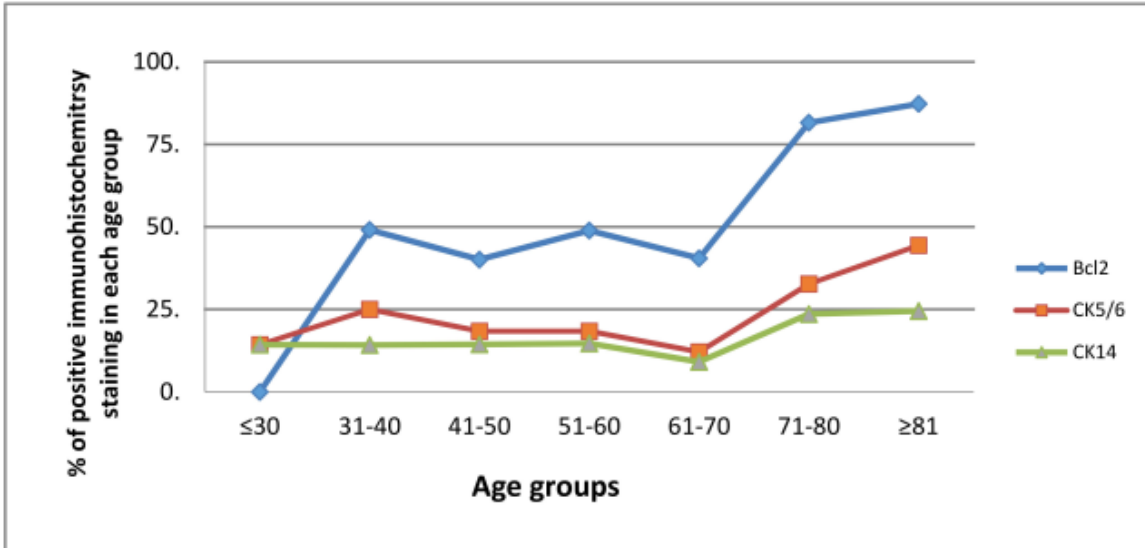
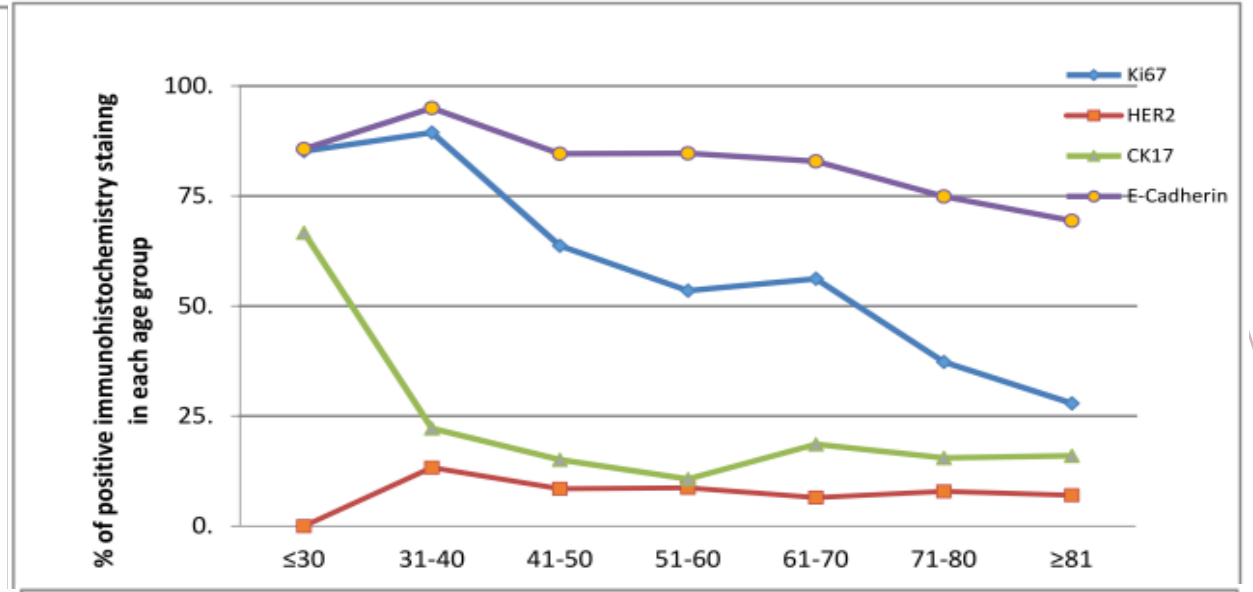
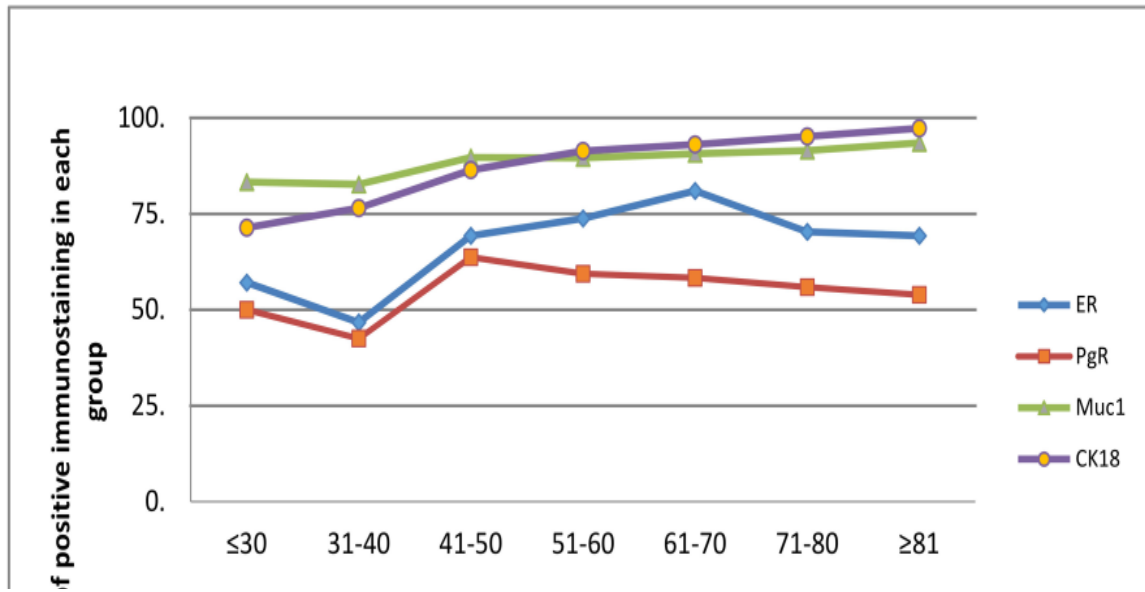
## Non métastatique

Breast cancer subtypes according to age determined by gene expression profiling

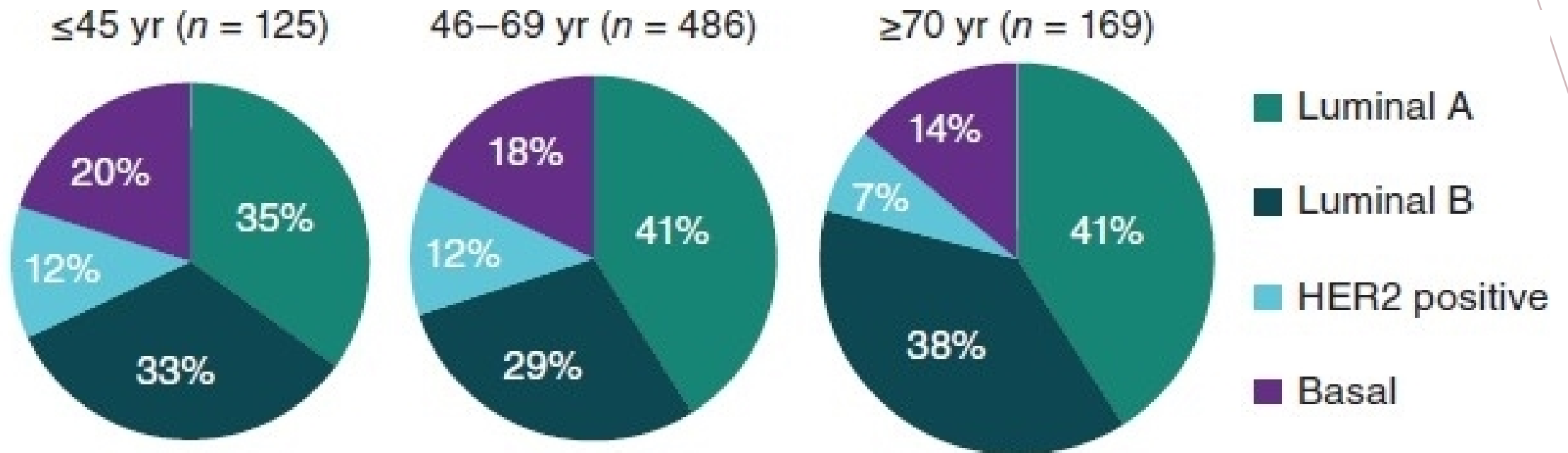


■ Luminal-A   
 ■ Luminal-B   
 ■ HER2   
 ■ Basal

# Répartition des sous-types histologiques en fonction de l'âge



# Répartition des sous-types histologiques en fonction de l'âge métastatique



# Répartition des mutations germinales BRCA

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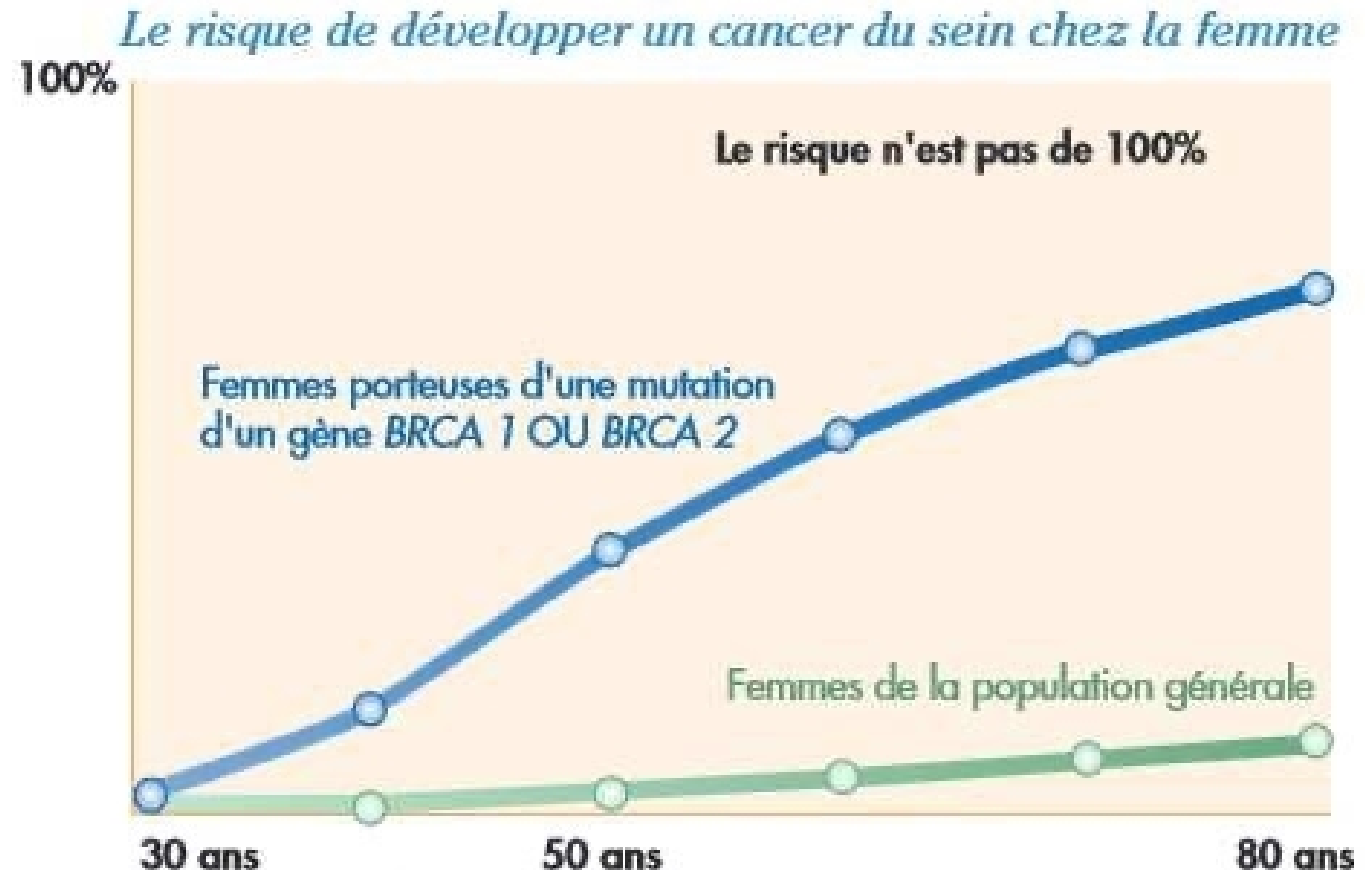
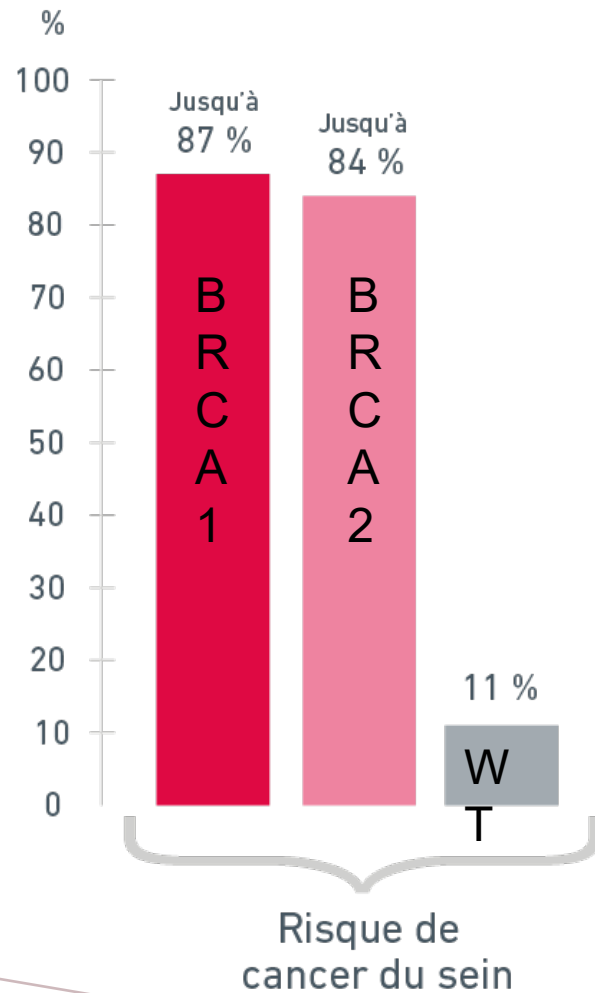
# Répartition des mutations germinales BRCA

|                                 | Ptes | Age      | BRCA1-2 |
|---------------------------------|------|----------|---------|
| <b>Ansquer Y</b><br>Lancet 1998 | 123  | < 36 ans | 12,4 %  |
| <b>Bonadona V</b><br>GCC 2005   | 47   | < 35 ans | 10,6 %  |
| <b>Esme</b><br>Unicancer        | 598  | ≤ 40 ans | 17 %    |

vs  
3,5%  
pour  
> 40 ans  
(Bonadon  
2005)



# Répartition des mutations germinales BRCA



# Répartition des mutations somatiques

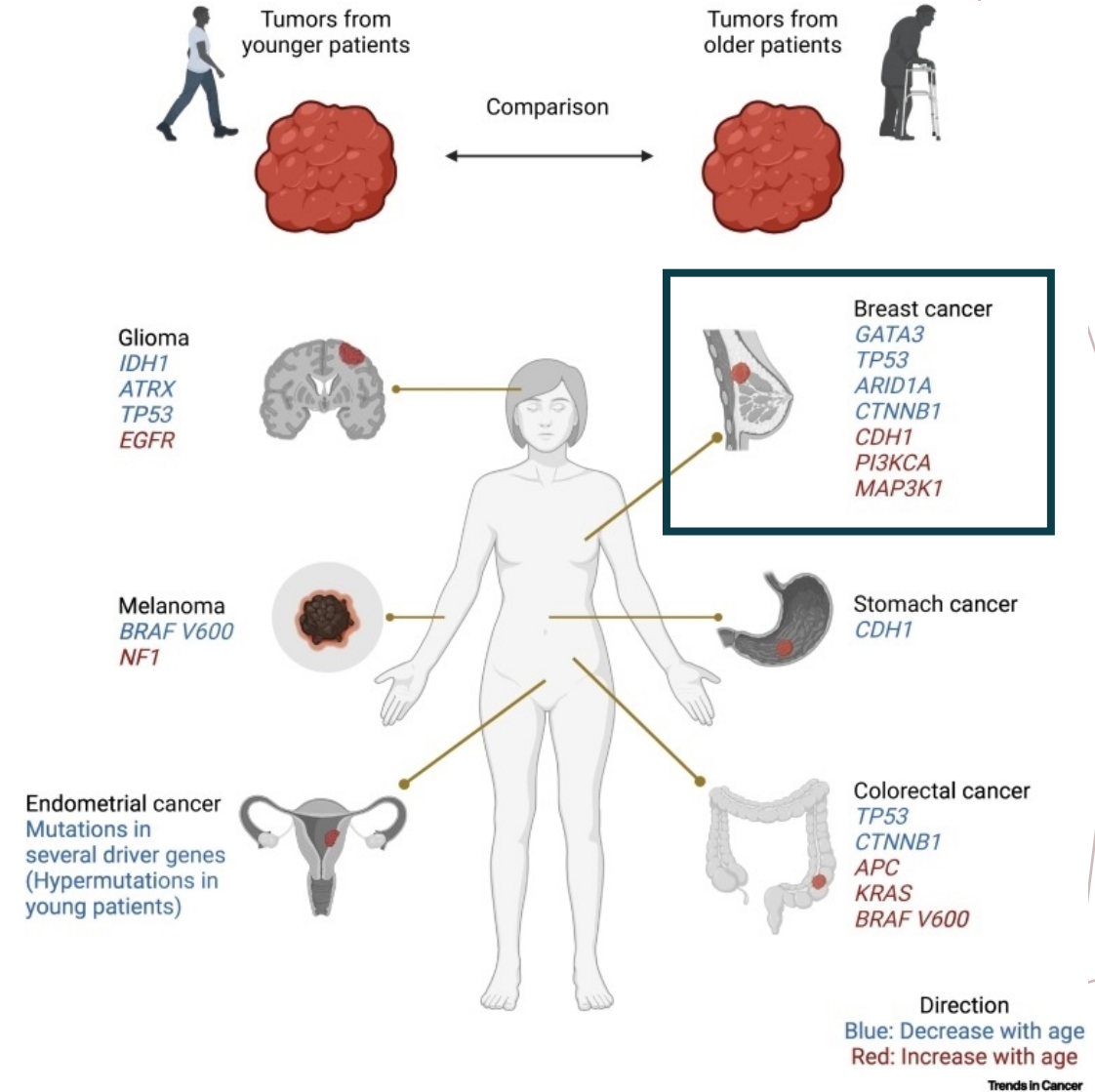
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# Répartition des mutations somatiques

Age groupe

| Gene          | ≤45  | 46–69 | ≥70  |
|---------------|------|-------|------|
| <i>GATA3</i>  | 15.2 | 8.2   | 9.0  |
| <i>TP53</i>   | 27.9 | 33.4  | 23.2 |
| <i>PIK3CA</i> | 28.8 | 32.7  | 41.9 |
| <i>TTN</i>    | 13.5 | 15.1  | 29.0 |

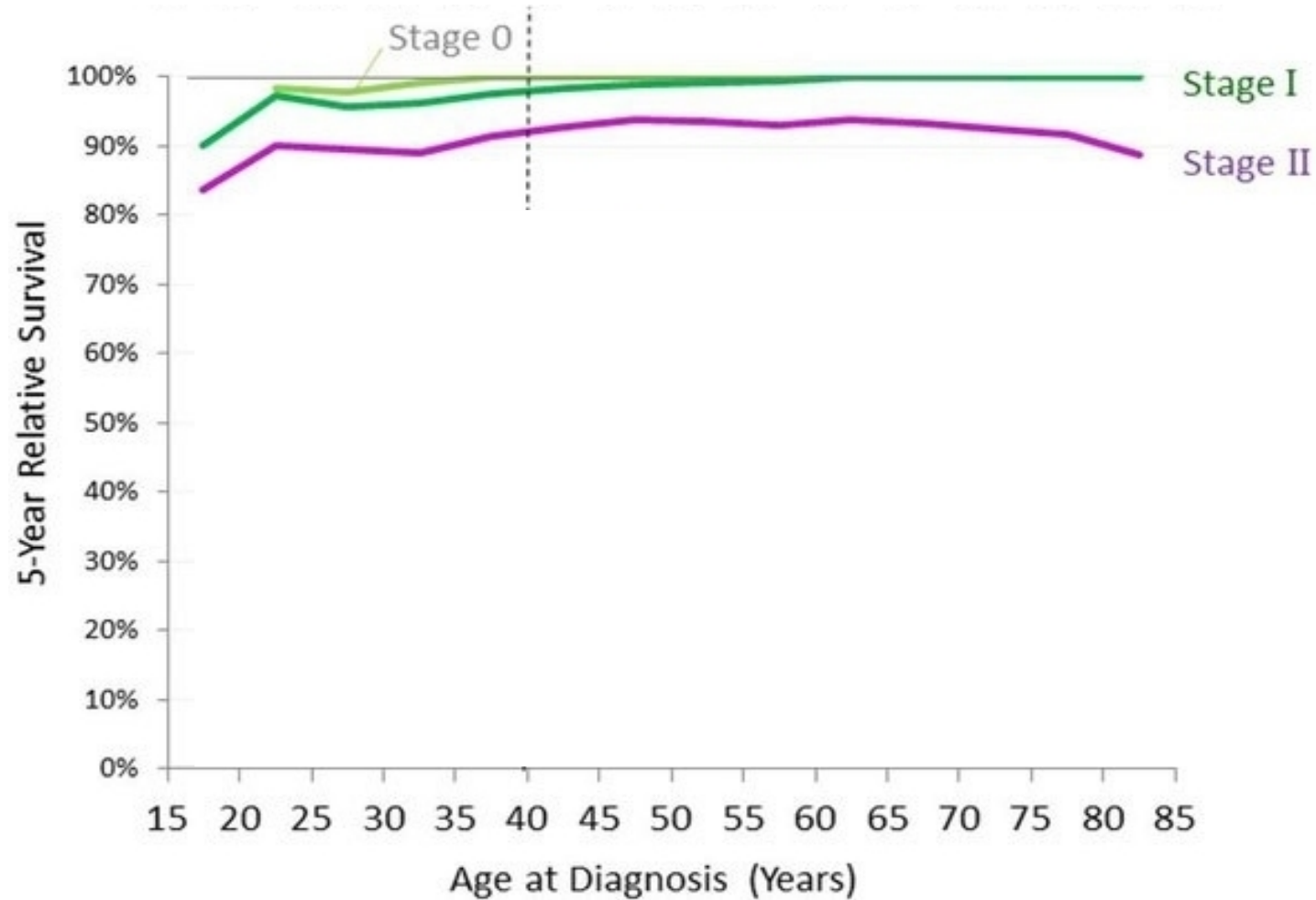
Prevalent somatic mutations (%) by age and intrinsic subtype, The Cancer Genome Atlas data set



# Valeur pronostique de l'âge

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# Valeur pronostique de l'âge



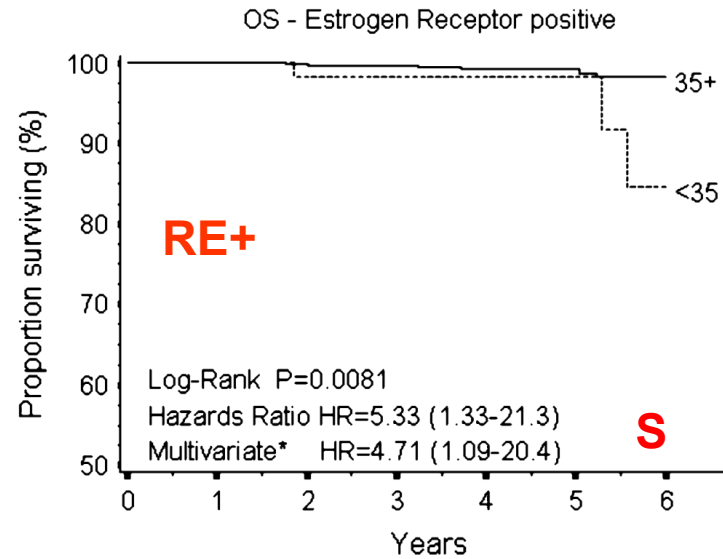
→ Pronostic défavorable pour les stades localisés

5-Year Relative Survival (lower panel) of Women with Invasive Breast Cancer, SEER18, 2000–2014, by Breast Adjusted AJCC6 Stage

# Valeur pronostique de l'âge en adjuvant

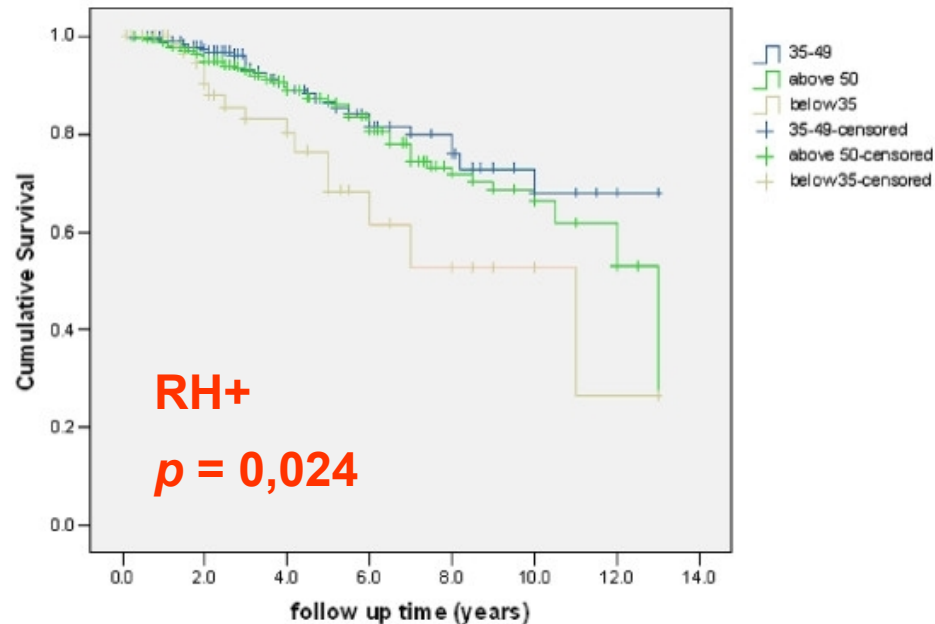
EIO 1997-2001  
841 patientes  
non ménopausées  
pN0

Colleoni et al, Ann Oncol 2006



1320 patientes  
dont 107 < 35 ans

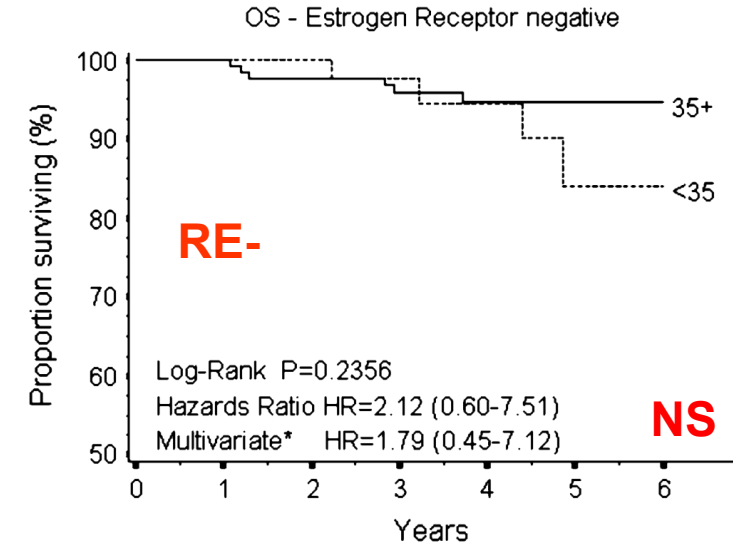
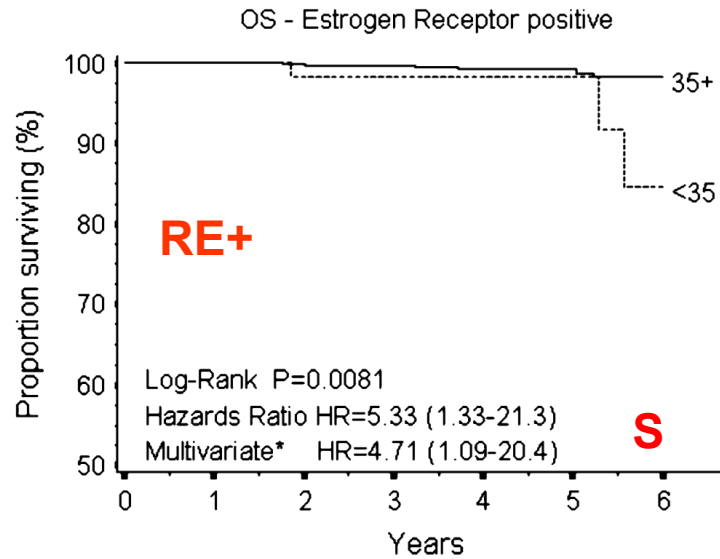
El Saghir et al, BMC Cancer 2006



# Valeur pronostique de l'âge en adjuvant

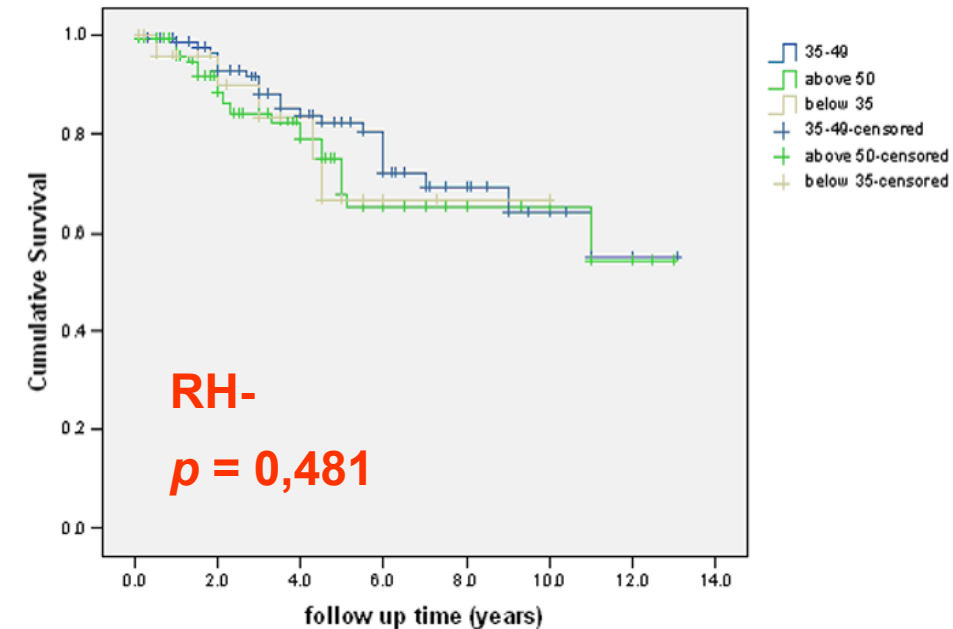
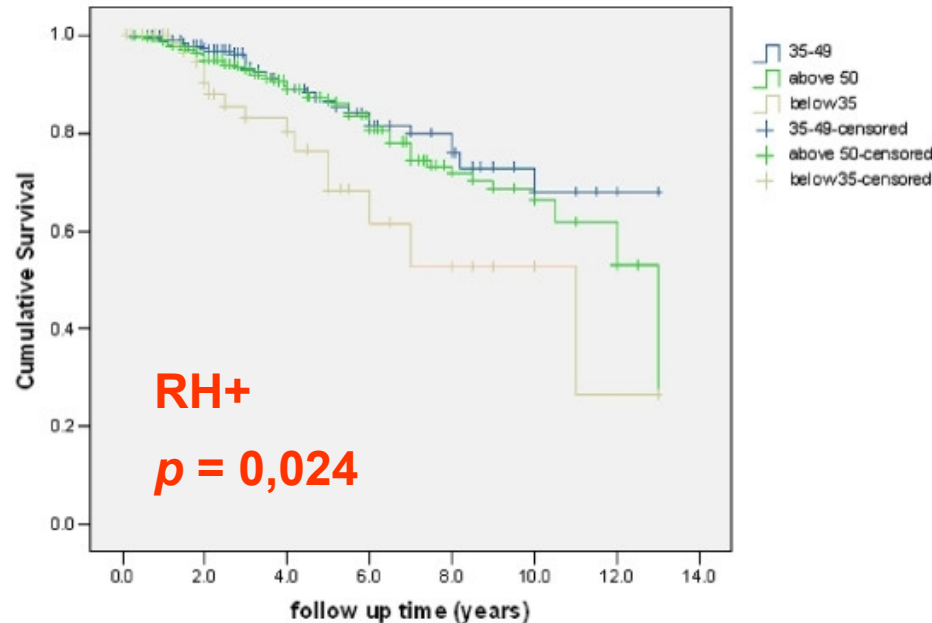
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841 patientes  
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pN0

Colleoni et al, Ann Oncol 2006

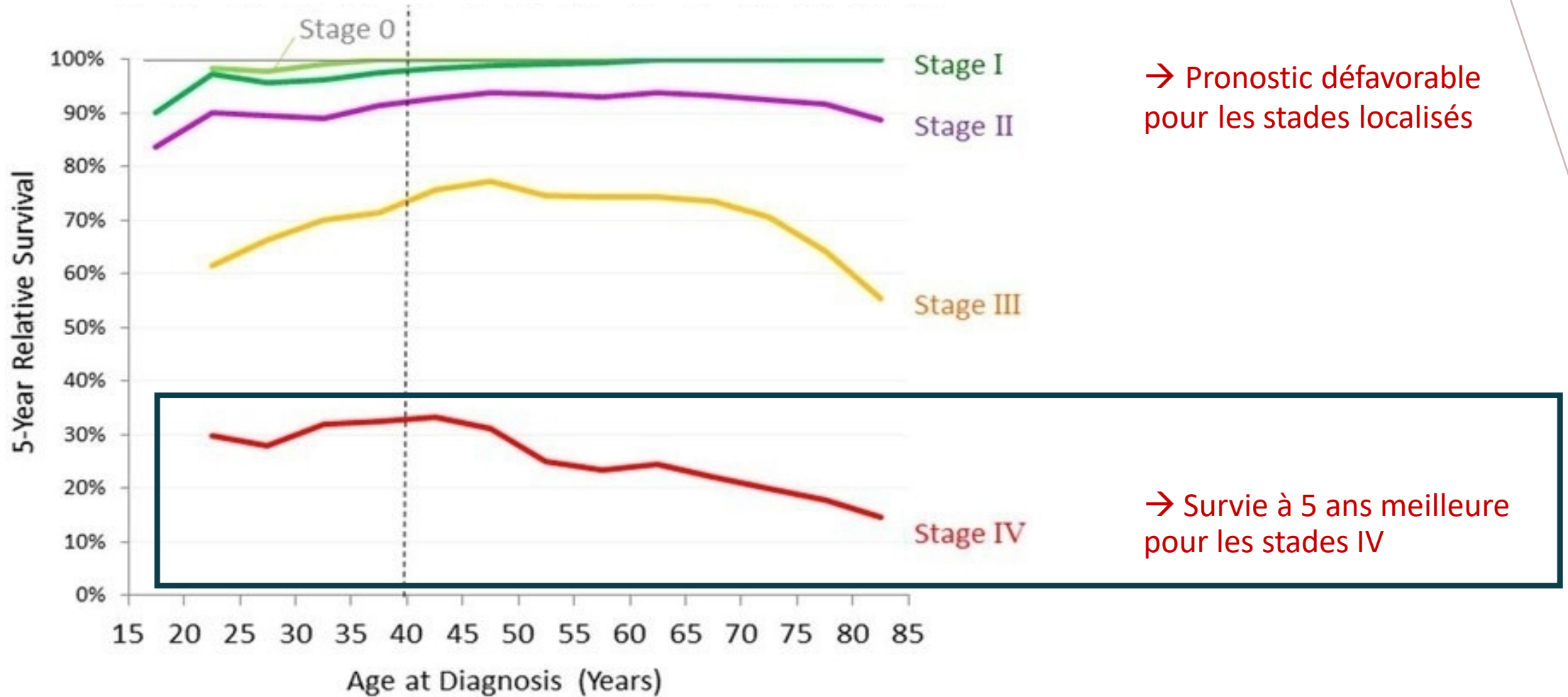


1320 patientes  
dont 107 < 35 ans

El Saghir et al, BMC Cancer 2006



# Valeur pronostique de l'âge



→ Pronostic défavorable pour les stades localisés

→ Survie à 5 ans meilleure pour les stades IV

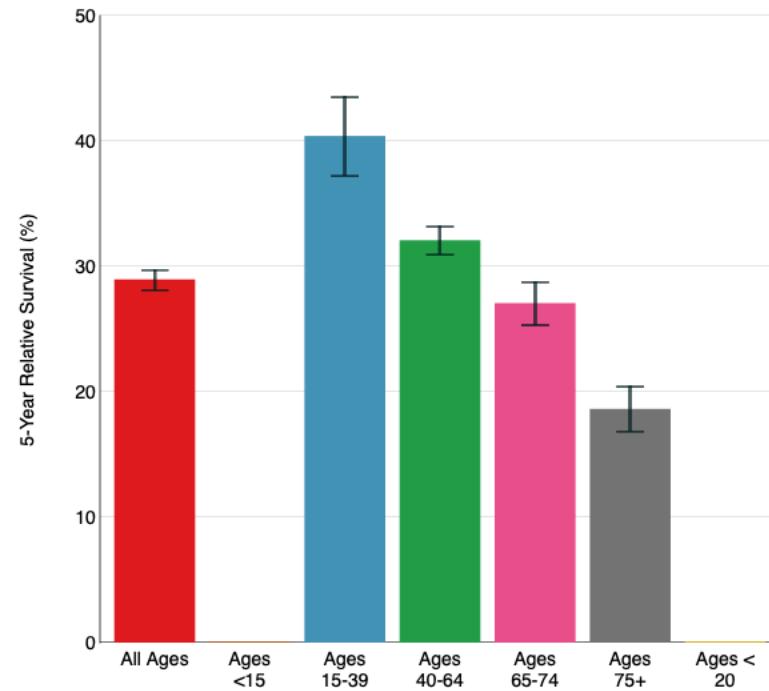
5-Year Relative Survival (lower panel) of Women with Invasive Breast Cancer, SEER18, 2000–2014, by Breast Adjusted AJCC6 Stage



# Valeur pronostique de l'âge en métastatique



**Breast**  
**SEER 5-Year Relative Survival Rates, 2011-2017**  
**By Age, Female, All Races (includes Hispanic), Distant**

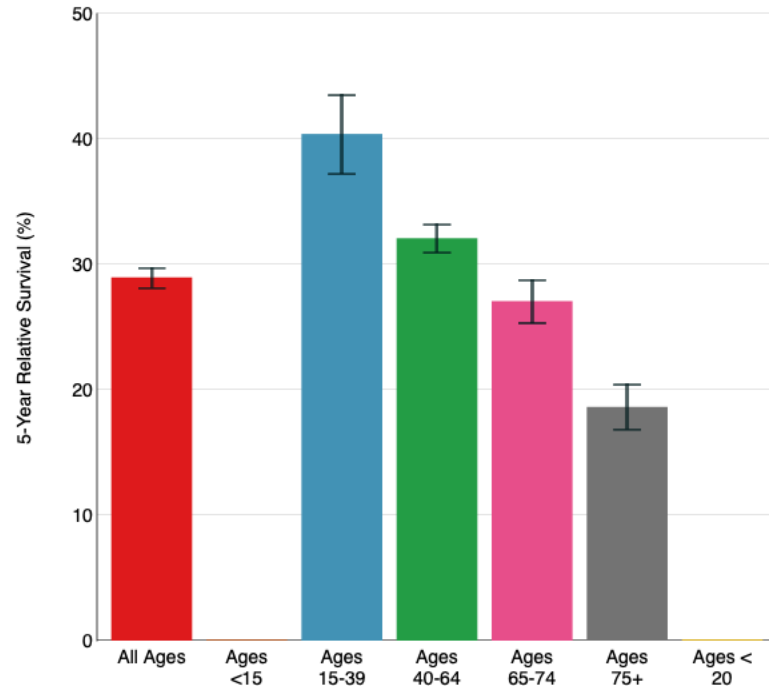


- Meilleure survie à 5 ans les patientes <40 ans
- Sous-types TN et HER2+

# Valeur pronostique de l'âge en métastatique



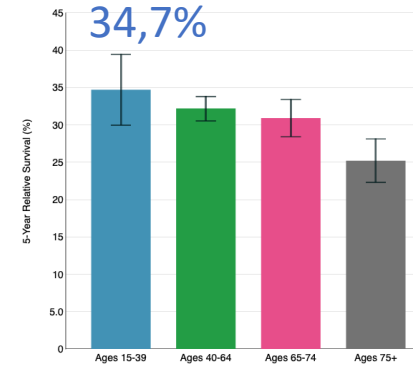
**Breast**  
SEER 5-Year Relative Survival Rates, 2011-2017  
By Age, Female, All Races (includes Hispanic), Distant



- Meilleure survie à 5 ans les patientes <40 ans
- Sous-types TN et HER2+

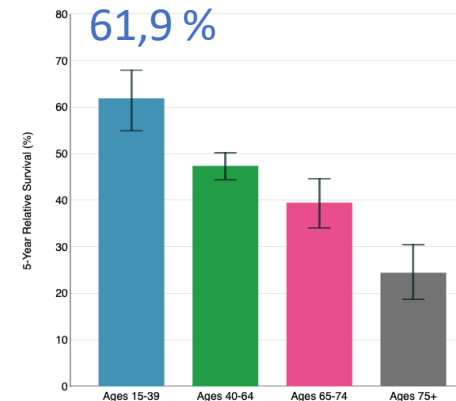
## RH+ HER2-

HR+/HER2- Breast Cancer (Female only)  
SEER 5-Year Relative Survival Rates, 2011-2017  
Female By Age, All Races (includes Hispanic), Distant



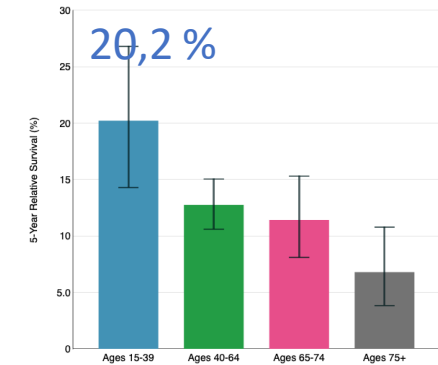
## RH+ HER2+

HR+/HER2+ Breast Cancer (Female only)  
SEER 5-Year Relative Survival Rates, 2011-2017  
Female By Age, All Races (includes Hispanic), Distant



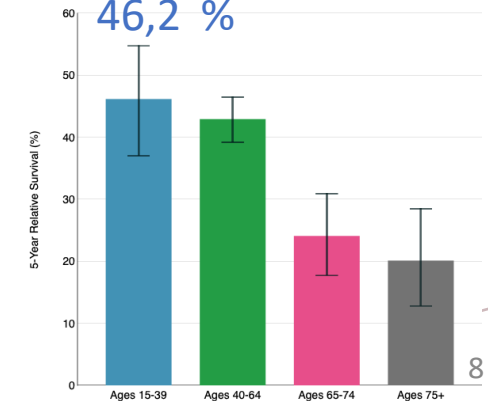
## TN

HR-/HER2- Breast Cancer (Female only)  
SEER 5-Year Relative Survival Rates, 2011-2017  
Female By Age, All Races (includes Hispanic), Distant



## RH- HER2+

HR-/HER2+ Breast Cancer (Female only)  
SEER 5-Year Relative Survival Rates, 2011-2017  
Female By Age, All Races (includes Hispanic), Distant



# Valeur pronostique de l'âge en métastatique



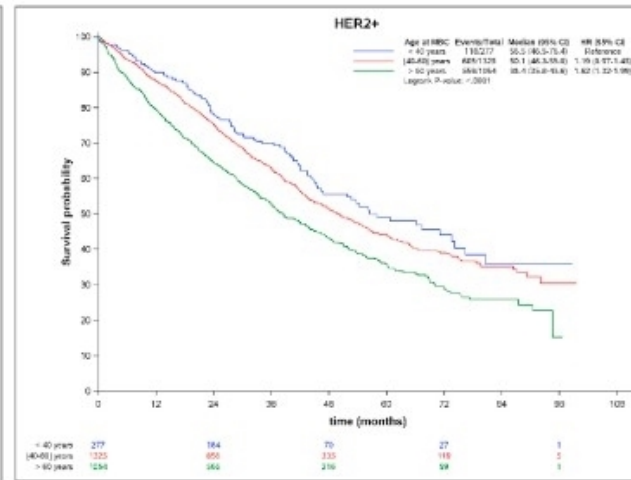
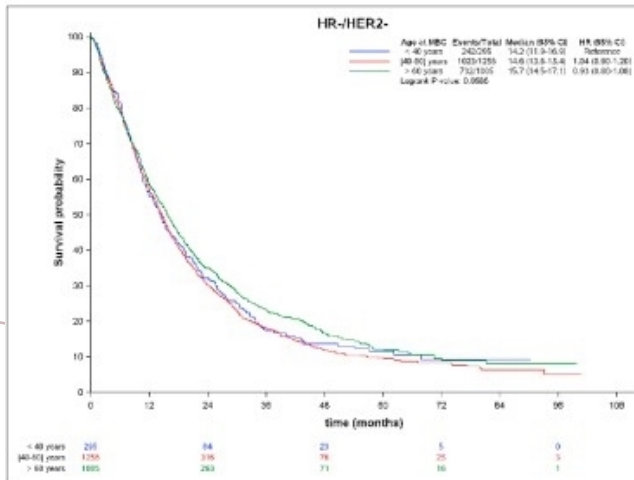
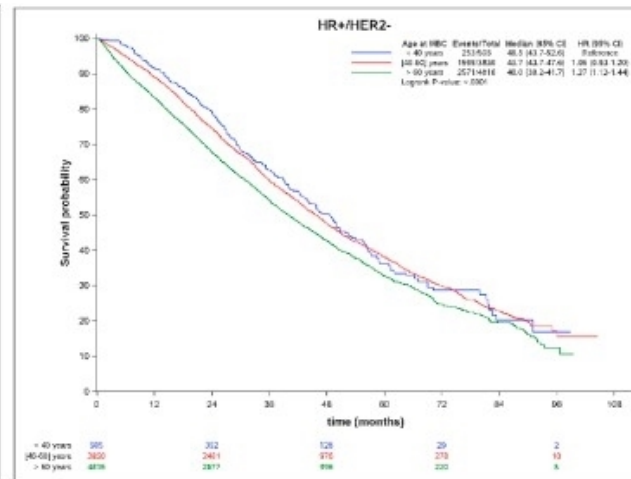
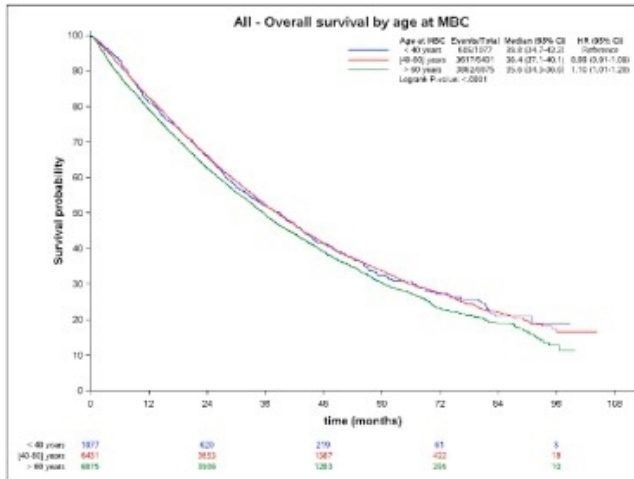
ESME MBC database  
1<sup>er</sup> Janvier 2008 au 31 Décembre 2014

14 403 ptes

**1077 (7,5%) <40 ans**

6436 (44,7%) 40-60 ans

6890 (47,8%) > 60 ans



→ Sous-types histologiques surreprésentés :  
HER2+ et TN

→ Survie identique pour les RH+  
→ Meilleure survie pour les HER2+

# Influence de l'âge sur le choix des traitements

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# Influence de l'âge sur le choix des traitements en adjuvant

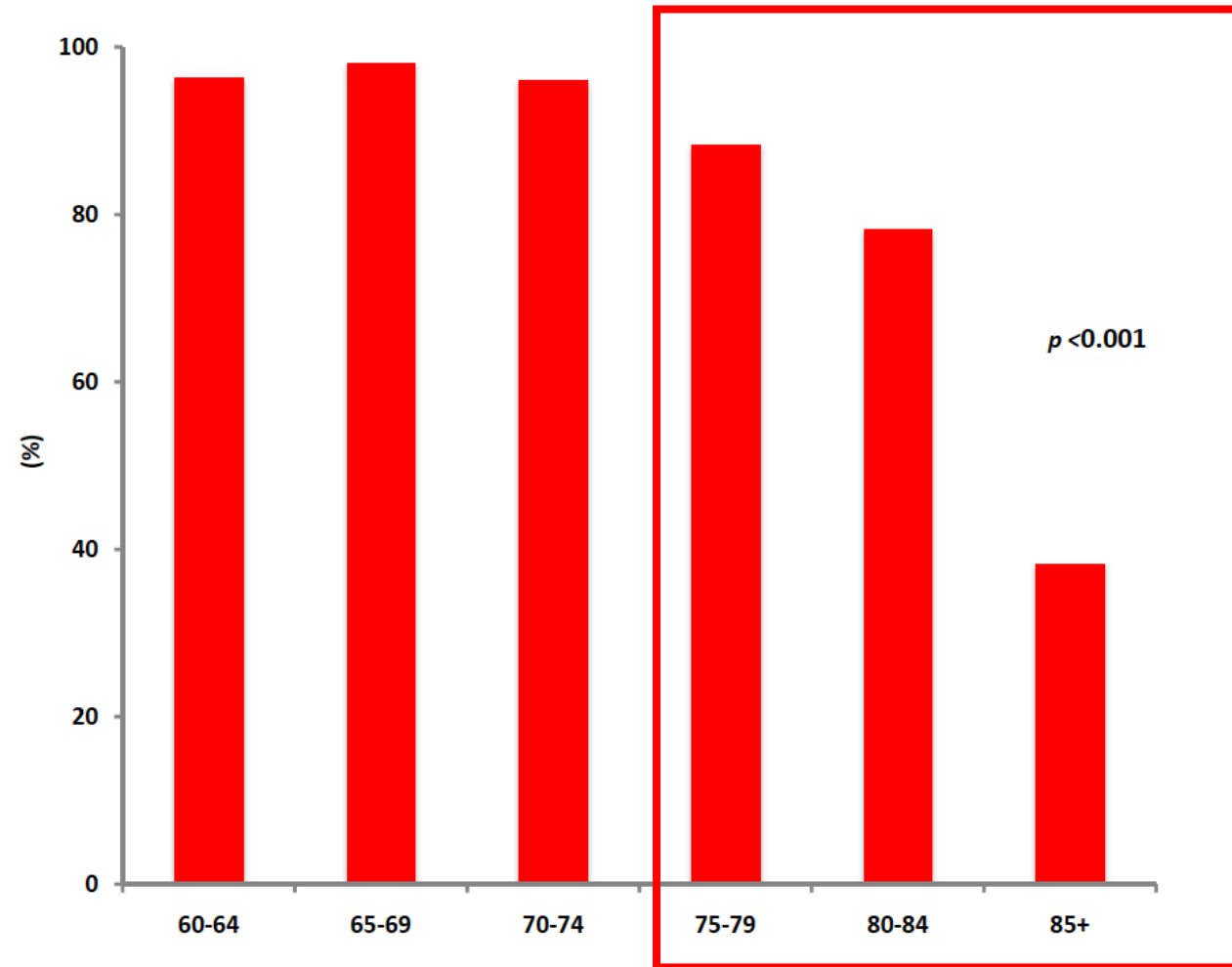


Figure 2: Percentage of women with stage 1 or 2 disease and a Charlson score of 0 who underwent surgery (n=850)

# Influence de l'âge sur le choix des traitements en métastatique

ESME MBC database

1<sup>er</sup> Janvier 2008 au 31 Décembre 2014

**Table 2**

Metastatic breast cancer characteristics according to age groups.

|  | All  |       | Age at MBC |       |               |       |           |       | P value between age groups |
|--|------|-------|------------|-------|---------------|-------|-----------|-------|----------------------------|
|  |      |       | <40 years  |       | [40–60] years |       | >60 years |       |                            |
|  | N    | %     | N          | %     | N             | %     | N         | %     |                            |
| <b>De novo MBC –treatment of primary tumor &lt;1y from diagnosis</b> |      |       |            |       |               |       |           |       |                            |
| Breast surgery   | 691  | 17.0% | 90         | 26.5% | 374           | 20.5% | 227       | 12.1% | 0.001                      |
| Loco-regional RT   | 1333 | 32.8% | 173        | 51.0% | 705           | 38.1% | 455       | 24.3% | <0.0001                    |

**Table 3**

First-line treatments according to tumor subtypes and age groups.

|                   | All  |       | Age groups (years) |       |       |       |      |       | P value between age groups |
|-------------------|------|-------|--------------------|-------|-------|-------|------|-------|----------------------------|
|                   |      |       | <40                |       | 40–60 |       | >60  |       |                            |
|                   | N    | %     | N                  | %     | N     | %     | N    | %     |                            |
| <b>HoR+/HER2</b>  |      |       |                    |       |       |       |      |       |                            |
| Chemotherapy      | 5456 | 58.1% | 418                | 80.5% | 2693  | 68.5% | 2345 | 47.4% | <0.0001                    |
| Endocrine therapy | 7358 | 78.3% | 364                | 70.1% | 2974  | 75.6% | 4020 | 81.3% | <0.0001                    |
| <b>Her2+</b>      |      |       |                    |       |       |       |      |       |                            |
| Chemotherapy      | 2469 | 89.5% | 273                | 95.5% | 1257  | 92.2% | 939  | 84.7% | <0.0001                    |
| Endocrine therapy | 1131 | 41.0% | 134                | 46.9% | 494   | 36.2% | 503  | 45.4% | <0.0001                    |
| Anti-Her2         | 2195 | 79.6% | 249                | 87.1% | 1115  | 81.7% | 831  | 75.0% | <0.0001                    |
| <b>HoR-/HER2-</b> |      |       |                    |       |       |       |      |       | <0.0001                    |
| Chemotherapy      | 2109 | 93.9% | 262                | 96.3% | 1092  | 96.0% | 755  | 90.2% | <0.0001                    |

# **PARTICULARITÉS DU CANCER DU SEIN INVASIF EN FRANCE CHEZ LA FEMME DE MOINS DE 40 ANS ET DE PLUS DE 70 ANS**



**Merci pour votre attention**

Dr BAILLEUX Caroline (Nice)  
SFSPM 2022