

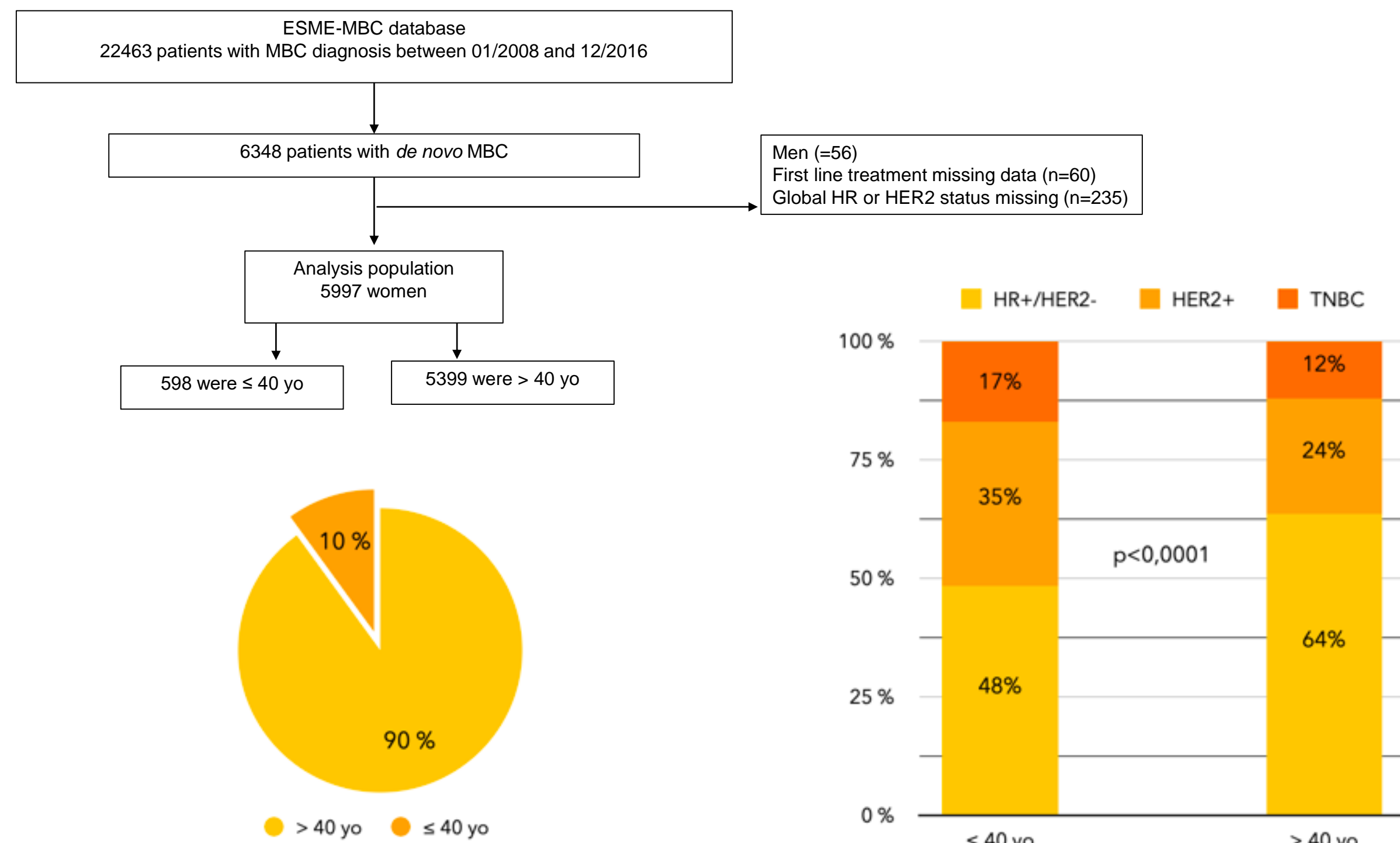
Introduction

Young women with breast cancer (BC), deserve a specific approach given peculiar issues including fertility, genetics and psychosocial concerns. *De novo* metastatic BC (MBC) in young women is a dramatic situation for which limited data are available.

Patients and methods

ESME is a unique French national multicenter cohort, collecting retrospectively data using clinical trial-like methodology. Using the ESME Data Platform, we evaluated the management and outcomes of women ≤ 40 yo diagnosed with *de novo* MBC. We compared the overall survival (OS) between young women and women > 40 yo, adjusted on main prognostic factors, globally and among the three major MBC subtypes.

Population disposition and distribution



Results

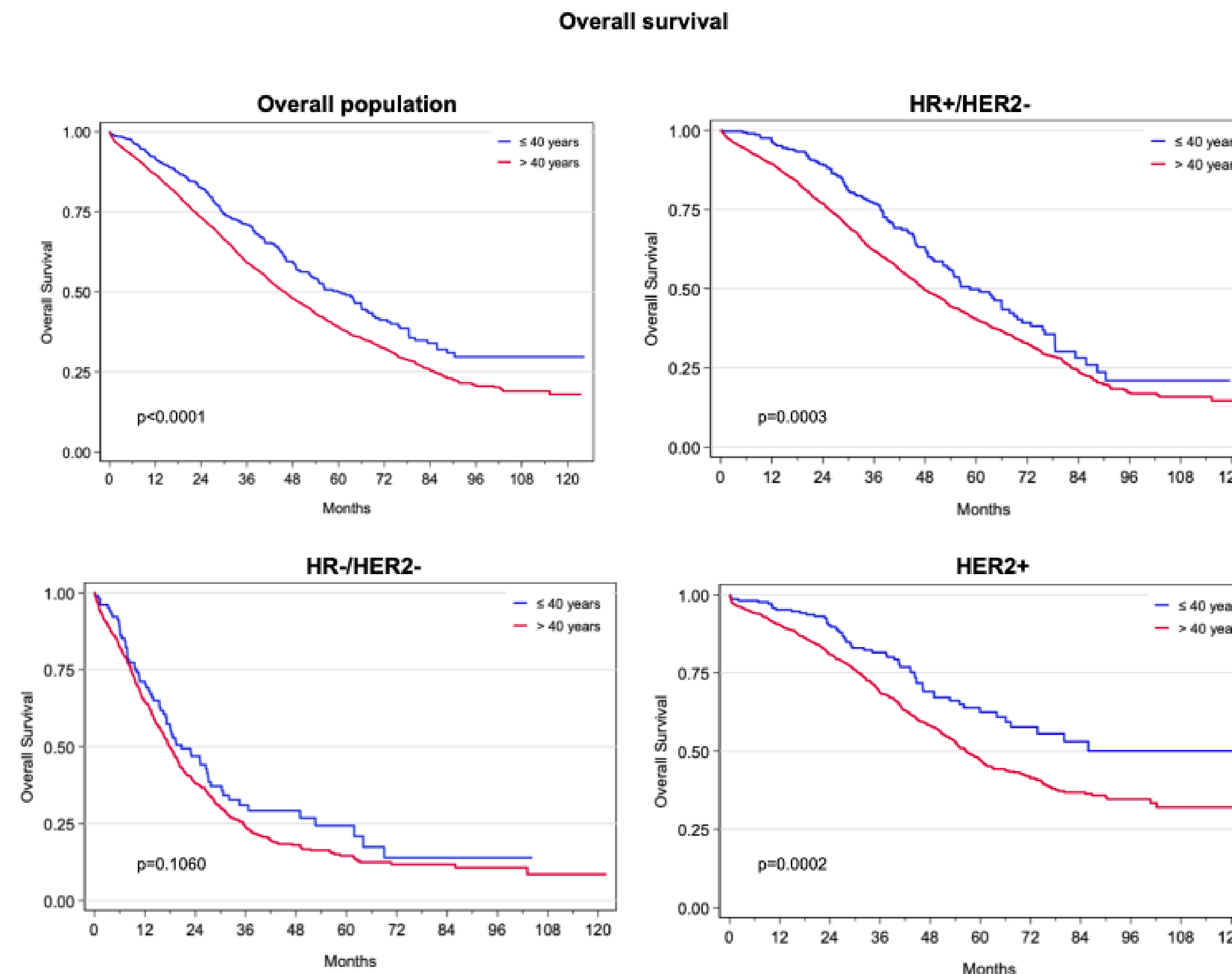


Figure 1 : Kaplan-Meier curves of overall survival (OS) in the whole cohort of patients and in each tumor subtype group by age at diagnosis

| Variable | Overall population | | HR+/HER2- | | HER2+ | | HR-/HER2- | |
|-----------------------------------|--------------------|------------|------------------|------------|------------------|------------|------------------|------------|
| | HR (95% CI) | p value | HR (95% CI) | p value | HR (95% CI) | p value | HR (95% CI) | p value |
| Age at diagnosis | | | | | | | | |
| ≤ 40 y | referent | — | referent | — | referent | — | referent | — |
| > 40 y | 1.41 (1.23-1.62) | < 0.0001 | 1.43 (1.18-1.74) | 0.0003 | 1.60 (1.21-2.11) | 0.0010 | 1.14 (0.86-1.50) | 0.3617 |
| Grade III | | | | | | | | |
| No | referent | — | referent | — | referent | — | referent | — |
| Yes | 1.14 (1.05-1.24) | 0.0018 | 1.20 (1.07-1.34) | 0.0012 | 1.08 (0.91-1.29) | 0.3719 | 1.03 (0.85-1.24) | 0.7639 |
| Number of metastatic sites | | | | | | | | |
| < 3 | referent | — | referent | — | referent | — | referent | — |
| ≥ 3 | 1.80 (1.63-1.99) | < 0.0001 | 1.53 (1.34-1.74) | < 0.0001 | 1.89 (1.54-2.33) | < 0.0001 | 2.66 (2.11-3.36) | < 0.0001 |
| Type of metastases | | | | | | | | |
| Visceral | referent | — | referent | — | referent | — | referent | — |
| Non visceral | 0.77 (0.70-0.84) | < 0.0001 | 0.70 (0.62-0.78) | < 0.0001 | 0.77 (0.62-0.95) | 0.0151 | 0.87 (0.71-1.07) | 0.1871 |
| Global subtype IHC | | | | | | | | |
| HR+/HER2- | Referent | — | — | — | — | — | — | — |
| HR-/HER2- | 2.79 (2.50-3.12) | < 0.0001 | — | — | — | — | — | — |
| HER2+ | 0.67 (0.61-0.75) | < 0.0001 | — | — | — | — | — | — |
| Global HR status | | | | | | | | |
| Négative | — | — | — | — | referent | — | — | — |
| Positive | — | — | — | — | 0.78 (0.65-0.93) | 0.0053 | — | — |

Table 1 : Multivariable cox model analysis of overall survival among subtype group

| Population | ≤ 40 y | | | | > 40 y | | | |
|--------------------|-------------|---------------------------|-----------------------------|---------------------------|--------------|---------------------------|-----------------------------|---------------------------|
| | N (%) | median OS months (95% CI) | median PFS1 months (95% CI) | 5-year OS rate % (95% CI) | N (%) | median OS months (95% CI) | median PFS1 months (95% CI) | 5-year OS rate % (95% CI) |
| Overall population | 598 (100%) | 59.9 (52.7-66.1) | 14.8 (13.3-17.0) | 49.8 (44.6-54.9) | 5399 (100%) | 45.9 (43.9-47.5) | 13.5 (12.9-14.0) | 39 (37.3-40.7) |
| HR+/HER2- | 289 (48.3%) | 58.5 (52.2-68.9) | 14.2 (12.8-16.7) | 49.8 (42.0-57.0) | 3430 (63.5%) | 47.6 (46.1-50.2) | 14.6 (14.0-15.3) | 40.4 (38.3-42.6) |
| HER2+ | 207 (34.6%) | not reached | 20 (16.3-24.2) | 62.5 (53.3-70.3) | 1314 (24.3%) | 56.5 (53.6-60.6) | 16.6 (14.7-17.9) | 47.1 (43.4-50.6) |
| HR-/HER2- | 102 (17.1%) | 20.7 (16.9-27.1) | 7.8 (5.5-11.3) | 24.4 (14.7-35.3) | 655 (12.1%) | 17.7 (16.5-19.6) | 6.4 (5.7-7.2) | 14.6 (11.3-18.4) |

Table 2 : Median OS, median PFS1 and 5-year OS rates in the overall population and within tumor subtypes

After a median follow up of 48.2 months, young women with *de novo* MBC had a better OS compared to older women. In multivariable analyses, age ≤ 40 y remained an independent favorable factor for OS in the whole population, in HR+/HER2- and in HER2+ population. To note, in HR+/HER2- patients, chemotherapy was selected as frontline treatment in the vast majority of young patients compared to older ones (89.6% versus 55.9% respectively, $p < 0.0001$).

Conclusion

In this real-life setting, 10% patients with *de novo* MBC are ≤ 40 yo. Young women had a significantly better OS compared to older ones, except for the TNBC subgroup in which results were similar. Age driving first-line strategy with various effects on outcome according to phenotype, specific questions regarding treatment choice are still relevant and should be addressed prospectively.

Acknowledgements / Funding

We thank all patients, participating centers and ESME Research Program funding sources (Roche, Pfizer, AstraZeneca, MSD, Eisai and Daiichi Sankyo).