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CLINICAL SCIENCE SYMPOSIUM Latest Practices in Follow up of Patients

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Trends in incidence, mortality, survival and treatment of primary invasive breast cancer in the Netherlands for women diagnosed between 1989–2017

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Background: During three last decades, the breast cancer (BC) landscape has changed considerably e.g. due to early-detection by screening and the more widespread use of (neo) adjuvant systemic treatments. The effects of these developments have influence on stage and treatment management, and trends in core epidemiological indicators and clinical management have hardly been studied. The aim of this study was to provide a comprehensive overview of the trends in incidence, mortality, survival and treatment of invasive BC, according to age, stage, and hormone receptor (HR)- and HER2 receptor-subtype in the Netherlands between 1989–2017.

Material and Methods: We selected all women aged ≥18 years diagnosed with primary stage I–IV BC between 1989–2017 from the nationwide population based Netherlands Cancer Registry (N = 320,249). BC mortality and reference population data were retrieved from Statistics Netherlands. Age-standardized incidence and mortality rates were calculated and joinpoint regression analysis was used to estimate average annual percentage changes. To estimate BC-specific survival, relative survival was calculated using the Ederer II method.

Results: BC incidence increased from 126 to 153 per 100,000 personyears between 1989 and 2017, but decreased annually for women aged \geq 75 since 1998 with -1.2% (95% confidence interval [CI]:-1.3, -1.1). For the total population, BC incidence decreased annually with -0.8% (95%CI: -1.1, -0.5) between 2013-2017. The incidence of stage I BC increased from 36 to 72 per 100,000 person-years between 1989–2017, whereas it decreased for stage II and III BC since 2004. Stage IV BC incidence remained stable around 8 per 100,000 person-years. Subtype-specific analyses showed that the incidence of HR+/HER2- and HR+/HER2+ BC increased annually with 0.7% (95%CI: 0.5, 0.9) and 1.0% (95%CI: 0.8, 1.3), respectively, between 2006–2017. The use of any (neo)adjuvant systemic treatment increased from 41.8% in 1989–1992 to 71.1% in 2013–2017, and combinations were provided more frequently. The use of breast conserving surgery and radiotherapy increased from 37.1% and 53.9% in 1989–1992, respectively, to 57.2% and 68.6% in 2013–2017. Mortality rates decreased from 57 to 35 per 100,000 person-years and relative survival improved for all ages, tumour stages and receptor-subtypes between 1989–2017. The five- and ten-year relative survival rates were 76.8% and 55.9% in 1989–1999, respectively, and increased to 92.0% and 84.8% in 2010-2017.

Conclusions: In the Netherlands, the incidence of primary invasive BC has steadily increased for most women since 1989, but the latest trends show promising declines. The use of (neo) adjuvant systemic treatments has increased considerably. Meanwhile, the mortality of invasive BC has decreased substantially and the survival has improved for all age groups, stages and receptor-subtypes.

No conflict of interest.

PLENARY SESSION

Keynote Lecture, Best and Late Breaking Abstract Presentations

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Clinical utility of MammaPrint testing in Invasive Lobular Carcinoma: Results from the MINDACT phase III trial

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Background: Chemotherapy-treatment (CT) decision for patients (pts) diagnosed with Invasive Lobular Carcinoma (ILC) remains controversial. We investigated the clinical utility of MammaPrint in pts diagnosed with early-stage ILC enrolled in MINDACT.

Material and Methods: MINDACT enrolled 6693 women with early-stage breast cancer and demonstrated the clinical utility of MammaPrint for adjuvant CT decision. This exploratory subgroup analysis includes pts with centrally-reviewed histologic data classified as IDC or ILC. Pts were categorized into risk groups based on MammaPrint for genomic risk (grisk) and modified Adjuvant!Online for clinical risk (c-risk). Pts with c-low/g-low risk were spared CT, while pts with c-high/g-high risk received CT. Discordant cases were randomized to receive CT based on the c- or g-risk.

Results: 5313 pts were included and centrally-classified as ILC (n = 487, including 255 classic ILC and 232 ILC variants) or IDC (n = 4826). 60.3% (395/654) of ILC cases by local assessment were confirmed by central pathology. 92 ILC cases by central review were classified differently by local assessment.

Compared to IDC, ILC tumors were larger (>2 cm, 41.1% vs 27.1%), more often ER+ (98.8% vs 87.7%) and less often HER2+ (3.5% vs 10.6%). 29.0% of ILC pts and 36.3% of IDC pts were premenopausal. Nodal status was balanced between groups (N1-3, 18.5% and 21.5% of ILC and IDC). 30.6% of ILC and 45.1% of IDC were treated with CT.

The C-risk classified 48.3% of ILC and 51.5% of IDC as c-high risk (cH). MammaPrint classified 16.2% of ILC and 39.1% of IDC as g-high risk (gH). In the subset of ILC, c- and g-risk were discordant in 6% cL/gH and 38% cH/gL and concordant in 45.8% cL/gL and 10.3% cH/gH.

MammaPrint classified 10.2% of classic ILC and 22.8% of ILC variants as gH. 5-yr DFS estimates was 93.0% (88.7; 95.7) for classic ILC and 88.4% (83.1; 92.1) for ILC variants.

| | | IDC | | ILC | |
|-----|------|------|-----------------------|-----|-----------------------|
| | | N | 5-year KM estimate | N | 5-year KM estimate |
| All | DMFS | 4826 | 94.9% (94.2; 95.5) | 487 | 95.5% (92.9; 97.1) |
| | DFS | | 90.4% (89.5; 91.2) | | 90.8% (87.6; 93.2) |
| gН | DMFS | 1888 | 92.3% (90.9; 93.5) | 79 | 89.4% (78.5; 94.9) |
| | DFS | | 87.1% (85.3; 88.6) | | 84.6% (73.5; 91.3) |
| gL | DMFS | 2938 | 96.5% (95.7; 97.2) | 408 | 96.6% (94.0; 98.1) |
| | DFS | | 92.5% (91.4; 93.4) | | 92.0% (88.6; 94.4) |

Conclusions: Compared to IDC, ILC tend to have higher tumor size, were more often ER-positive and less often HER2+. ILC and IDC had a similar distribution of c-risk, while 16% of ILC were high g-risk, with unfavorable survival outcomes. 38% ILC pts classified as c-high/g-low risk.

Higher rates of gH and lower DFS rate were observed in ILC variants than in classic ILC.

DMFS and DFS estimates were similar for ILC and IDC classified as either low or high-g-risk, suggesting that MammaPrint also has prognostic value in ILC and may be a clinically useful tool for adjuvant treatment decision making in ILC.