Nationwide evaluation of breast cancer biomarker assessment in daily practice

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Nice

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Disclosure Information

I hereby declare that I have no conflict of interest
Content

• Hormone- and HER2-receptor assessment in 33,046 breast cancer patients: a nationwide comparison of positivity rates between pathology laboratories in the Netherlands

• Significant inter- and intra-laboratory variation in grading of invasive breast cancer: a nationwide study of 33,043 patients in the Netherlands
Breast cancer: background

• Most common type of cancer in European women\(^1\)

• Breast cancer management: *it all starts with pathology*
  – Subtype: PATHOLOGY
  – Prognosis: PATHOLOGY
  – Treatment: PATHOLOGY

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1. International Agency for Research on Cancer (WHO), source: GLOBOCON 2018
Breast cancer biomarkers

- **Receptor-assessment**
  - ER, PR, HER2

- **Histologic grade**
  - B&R (modified)

- **Clinical decisions**
  - Anti-endocrine therapy
  - Anti-HER2 therapy

- **Clinical decisions**
  - Chemotherapy
  - Radiotherapy
  - Gene-expression profiling
Reproducibility of breast cancer biomarkers

• Receptor assessment: significant differences\textsuperscript{1-16}
• Histologic grading: no more than moderate\textsuperscript{16-19}

But how are we doing in daily clinical practice?

Real-life data on a Dutch nationwide level

the nationwide network and registry of histo- and cytopathology in the Netherlands

- Synoptic reporting

1. PALGA Foundation, Annual Report 2018
Breast cancer biomarkers

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Receptor assessment: clinical decisions

• **ER/PR**
  – IHC
  – 10% cut-off
  – Anti-endocrine therapy

• **HER2**
  – IHC
  – 10% cut-off
  – Amplification testing (IHC 2+)
  – Anti-HER2 therapy
Receptor assessment: quality control

• External audits mandatory

• Temporary and incomplete assessment of testing performance?*
  – Tissue fixation
  – Tissue processing

• Surveillance of positivity rates as new tool to identify outlying laboratories?

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ER-assessment in the Netherlands; 2013-2016 (n=33,794)
Laboratory-level (n=39)

Data adjusted for age, tumour size, type of surgery, histologic subtype, histologic grade, HER2-receptor status
PR-assessment in the Netherlands; 2013-2016 (n=33,794)
Laboratory-level (n=39)

Mean: 71.3%
Range: 62.5-77.5%

Data adjusted for age, tumour size, type of surgery, histologic subtype, histologic grade, HER2-receptor status
HER2-assessment in the Netherlands; 2013-2016 (n=33,794)
Laboratory-level (n=39)

Mean: 9.9%
Range: 5.5-12.7%

Data adjusted for age, tumour size, type of surgery, histologic subtype, histologic grade, ER/PR-receptor status
Conclusion: ER, PR, HER2 assessment

• Synoptic pathology reports of >33,000 patients

• Absolute variation for ER, PR and HER2 is limited

• Considerable number of outliers (PR)
  – Feedback reports: creating awareness
Breast cancer biomarkers

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Grading in the Netherlands; 2013-2016 (n=33,792)
Laboratory-level (n=39)

Case-mix: age, tumour size, type of surgery, histologic subtype, ER/PR- and, HER2-receptor status
Grading in the Netherlands; 2013-2016 (n=33,792)
Laboratory-level (n=39)

Grade II

Proportion (%) grade II
Number of IBC reports per laboratory

Grade III

Proportion (%) grade III
Number of IBC reports per laboratory

Mean: 47.6%
Range: 38.4-57.8%

Mean: 24.3%
Range: 15.5-34.3%
Grading in the Netherlands; 2013-2016
Pathologist-level (n=68, 8 laboratories)
Grading in the Netherlands; 2013-2016
Pathologist-level (n=68, 8 laboratories)

Grade II

Grade III
Grading variation; does it really matter?

Chemotherapy (n=19,461)

According to the Dutch breast cancer guideline, adjuvant chemotherapy (aCT) is advised for patients with a positive lymph node status (N+), and for patients with a negative lymph node status (N0) with the following characteristics:

- Age < 35 years, except for a grade I tumor < 1 cm
- Age ≥ 35 years with a tumor of 1.1-2 cm and ≥ grade II, or a tumor > 2 cm
- HER2 overexpression in a tumor ≥ 0.5 cm

N0: n=13,077
N+: n=6,384
HER2+: n=1,119
HER2-: n=11,958

Grade I: no aCT
Grade II-III: aCT

Conclusion: histologic grading

- Synoptic pathology reports of >33,000 patients

- Substantial inter- and intra-laboratory variation in grading of invasive breast cancer in daily clinical practice
  - Not explained by differences in case-mix

- Biomarker of major clinical importance
  - Decrease in variation warranted

- Interventions
  - Feedback reports
  - E-learning
Breast cancer biomarkers in daily practice

Receptor-assessment

- ER, PR, HER2
- Limited absolute variation
- Considerable number of outlying laboratories (PR)
  - Feedback reports?

Histologic grading

- B&R (modified)
- Substantial variation between and within laboratories
- Interventions
  - Feedback reports: effect?
  - E-learning: effect?
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