Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Prognostische und prädiktive Faktoren
Data bases screened

Guidelines screened
3. NCCN 2016: www.nccn.org

Definition

Ein **prognostischer Faktor** ist ein Parameter, der zu einem interessierenden Zeitpunkt z.B. bei Erstdiagnose vorliegt und, sofern keine weitere Therapie erfolgt, mit dem krankheitsfreien oder dem Gesamtüberleben d.h. mit dem natürlichen Krankheitsverlauf korreliert.

Ein **prädiktiver Faktor** ist ein Parameter, der das Ansprechen auf eine bestimmte Therapie definiert.

* Im Sinne dieser Leitlinie gemeint sind Faktoren, die mit einem Krankheitsrezidiv assoziiert sind.


Requirements for a Marker-Based Test to Reach Level IB Evidence

- 1. Adequate amounts of archived specimen must be available from enough patients from a prospective trial ... for analyses to have adequate statistical power and for the patients included in the evaluation to be clearly representative of the patients in the trial.
- 2. The marker-based test should be analytically and preanalytically validated for use with archived specimens.
- 3. The plan for marker evaluation should be completely specified in writing before the performance of marker assays on archived specimens and should be focused on evaluation of a single completely defined marker-based test.
- 4. The results from archived specimens should be validated using specimens from one or more similar, but separate, studies.

McShane & Hayes, J Clin Oncol 30: 4223-4232, 2012


Statement: Obesity


pCR after NACT


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**Reproducibility**

- ER/PR: concordance central vs local is high (97%; Plan B, SABCS 2014)
- Grading: concordance central vs local is 68% (PlanB, JCO 2016)
- HER2: frequency of false-positive test results 6% (ASCO /CAP JCO 2013)
- Impact of routine pathologic review in N0 BC: 20% changes : grading 40%, LVI 26%, N 15%, margin 12% (JCO 2012)
- pN0 from MIRROR study: pN0 was upstaged in 22%, in central pathology review (Ann Oncol 2012)
- Inter- and intraobserver variability in measurement of ki-67 is high (J Nat. Cancer Institute 2011)
2013, 31(31):3997-4013.


Ki-67


Post-treatment Ki-67


uPA/PAI-1
ER/PR


HER2


Ki-67


Post-treatment Ki-67


uPA/PAI-1
Endopredict


**Mammaprint**


Oncotype


Prosigna (ROR / PAM50)


Multiple assays

Endopredict


**MammaPrint**


Oncotype


**Prosigna (ROR / PAM50)**


Multiple assays

Mammaprint


Oncotype DX


Several tests

Oncotype DX

Oncotype DX


**DTC and radiation**


CTC

Oncotype


Endopredict


6. Dubsky, San Antonio 2017


**Prosigna (ROR, PAM50)**


10. Sestak I, Cuzick J, Dowsett M, et al. Prediction of Late Distant Recurrence After 5 Years of Endocrine Treatment: A Combined Analysis
of Patients From the Austrian Breast and Colorectal Cancer Study Group 8 and Arimidex, Tamoxifen Alone or in Combination Randomized Trials Using the PAM50 Risk of Recurrence Score. J Clin Oncol. 2014 Oct 20. pii: JCO.2014.55.6894

Mammaprint


Lobular cancer

1. Loibl S, Volz C, Mau C, et al. Response and prognosis after neoadjuvant chemotherapy in 1,051 patients with infiltrating lobular...
TIL


Denkert et al, SABCS 2016

**PIK3CA**


CYP2D6
OncotypeDX


uPA/PAI-1


CTC


Cell-free DNA


CTC monitoring


PARP-Inhibitoren


Checkpoint-Inhibitoren
Commercially Available Comprehensive Molecular Profiling Tests


Exome/Whole Gene Testing of Panel Genes or the Whole Genome (Genomic Profile Tests)

<table>
<thead>
<tr>
<th>Provider</th>
<th>Local Pathology based*</th>
<th>Foundation one*</th>
<th>Molecular Health Guide*</th>
<th>NeoSelect*</th>
<th>GPS Cancer*</th>
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<tbody>
<tr>
<td>LocalPathologist</td>
<td>Roche</td>
<td>Molecular Health</td>
<td>Siemens Healthineers</td>
<td>NanHealth</td>
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<tr>
<td>Number of Genes</td>
<td>&gt;300</td>
<td>&gt;600</td>
<td>39</td>
<td></td>
<td>whole genome</td>
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<tr>
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<td>yes</td>
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<td>yes/yes</td>
<td>yes</td>
<td>yes</td>
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<td>Indication and population studied</td>
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<tr>
<td>Registration / QM</td>
<td>Local QC Standards, Analyse „CE konform“</td>
<td>FDA approved</td>
<td>ISO13485</td>
<td>„CE-konform“</td>
<td>CLIA certified CAP accredited</td>
</tr>
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</table>

* Interpretation of genomic alterations with regard to resistance or efficacy of therapies, eligibility for clinical trials etc. by bioinformatic, automated, quality controlled algorithms (e.g. OncoKB.org)
** Implemented in molecular tumor boards as part of clinical routine
*** some of which are professionalized like MSK-IMPACT (FDA authorized)


10. Tutt APE, Kilburn L, Gilett C, et al. The TNT trial: A randomized phase III trial of carboplatin (C) compared with docetaxel (D) for patients with metastatic or recurrent locally advanced triple negative or BRCA1/2 breast cancer (CRUK/07/012). DOI: 101158/1538-7445SABCS14-S3-01 Published May 2015 2015.


**PIK3CA**


