Factors Influencing Selection of Systemic Therapy for Primary Breast Cancer

- Risk of recurrence or death
- Benefit from treatment
- Comorbidities
- Toxicities
- Tumor characteristics: ER, PR, HER-2

Optimal treatment selection
Molecular Diagnostics in Breast Cancer: Past, Present and Future Technologies

XIX century 1980s 2000 XXI century (?)

Histology Single gene predictors Multi-gene predictors (?)

DNA arrays SNP analysis Multiplex PCR Proteomics

Historical Evolution of Biomarkers for Breast Cancer

Histopathology
- Tumor size
- Lymph node involvement
- Grade
- Tumor type
- Lymphovascular invasion

Single Molecular Markers
- Estrogen receptor
- Progesterone receptor (?)
- HER-2
- Ki-67

Prognostic Indices
- Nottingham Prognostic Index
- Adjuvant!
- Composite expert opinion
- uPA/PAI-1

Gene Expression Microarrays:
- MammaPrint
- VDX2 array
- Oncotype DX
- 97-gene genomic grade index
- Intrinsic subtypes

Predictive Indices:
- HOXB13:IL17RB
- 200-gene ER reporter index
- 97-gene genomic grade index
- Multigene predictors of docetaxel, paclitaxel, AC, EC, paclitaxel-FAC

High throughput methods

Gene Expression Microarrays:
- MammaPrint
- VDX2 array
- Oncotype DX
- 97-gene genomic grade index
- Intrinsic subtypes

Predictive Indices:
- HOXB13:IL17RB
- 200-gene ER reporter index
- 97-gene genomic grade index
- Multigene predictors of docetaxel, paclitaxel, AC, EC, paclitaxel-FAC
When is a test ready for clinical use?

- Assay measurements have to be reproducible and robust.
- The predictor must be fully defined (including cut off values).
- The predictive performance of the test has to be validated on independent cases that are clinically relevant (PPV, NPV, Sensitivity, Specificity).

Technically sound test with known accuracy = provides reliable information

- Is the new predictor better than the current best method to predict the same outcome?
- Does the use of the test improve clinical outcome?

Development of Adjuvant!online

- **Factors considered:**
  - Age
  - Comorbidity
  - Estrogen Receptor (ER) status
  - Tumor grade
  - Tumor size
  - Number of positive nodes
  - Factor selected by user
- **Endpoints:**
  - Relapse
  - Mortality

- **Treatments considered:**
  - Endocrine therapy
    - Tamoxifen
    - Aromatase inhibitors
    - Tamoxifen + AI
    - Ovarian ablation
    - OA + tamoxifen
  - Chemotherapy
    - CMF (overview)
    - Anthracycline (overview)
    - 1st generation regimens
    - 2nd generation regimens
    - 3rd generation regimens

Population-Based Validation of the Prognostic Model
ADJUVANT! For Early Breast Cancer

Olivotto IA, et al
J Clin Oncol
23(12):2716-25, 2005
Gene expression array-identified subtypes of Breast Cancer

Unsupervised Hierarchical Clustering of Primary Breast Cancers


Hierarchical Clustering Analysis of 184 Breast tumors, 9 normals and 12 Metaplastic carcinomas

Hennessy B., et al. *Cancer Cell 2008*

Claudin gene set cluster

Basal gene set

Proliferation gene set

Luminal/ER+ gene set

HER2-amplicon gene set
Are DNA microarray measurements reproducible enough for clinical use?

**US FDA Microarray Quality Control Project**

- 4 different RNA samples (A,B,C,D), 5 replicates for each, at 3 sites, for 6 commercial platforms.

**Signal variation (CV%)**
- of 5 replicates within one laboratory

**Signal variation (CV%)**
- of 5 replicates across 3 different laboratories

**Reproducibility of signal for 6 commercial platforms**


**Correlation between RT-PCR and microarray-based gene expression measurements.**

**Correlation between Affymetrix measurements and Taq-Man results**

Scatter plots of log ratios of signal (Sample A over sample B, n=451-472 genes)

Properly performed microarray-based mRNA measurements can be as reliable as Taq-Man! However dynamic range is smaller!

A gene expression signature of good prognosis

Each column is a gene (n=70)*
Each raw is a tumor profile (n=78)

70-gene MammaPrint™ signature (Agendia Inc)

(Partial) Validation results on n=296 patients
Validation results on n=303 patients

Do multigene genomic tests add to current clinical variable based prediction models?

76-gene prognostic signature (Veridex Inc)

**Discovery:** n=115, node-negative patients, no adjuvant therapy

**Validation on Independent samples**

**Split sample validation, n=171**

- 10-yr DMFS 94% (95%CI: 83-98%)
- 10-yr DMFS 65% (95%CI: 53-74%)

**Independent validation, n=180**

- 10-yr DMFS 94% (95%CI: 83-98%)
- 10-yr DMFS 65% (95%CI: 53-74%)

**10-yr DMFS 94% (95%CI: 83-98%)**

**64%**

**Low risk by Adjuvant**

**67%**

**High risk by Adjuvant**

**Discordance rates clinical vs MammaPrint**

**There is an about 30% discordant risk prediction between Adjuvant Online and MammaPrint!**

**Which is better or are they complementary?**
These results are only applicable to node negative patients. The numbers in each group are small therefore confidence intervals are relatively broad!


Association Between the “Invasiveness” Gene Signature and Survival in Patients with Breast Cancer

Table 4. Risk of Death or Metastasis among Patients with Breast Cancer (Multivariate Analysis).\(^a\)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Death</th>
<th></th>
<th>Metastasis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard Ratio (95% CI)</td>
<td>P Value</td>
<td>Hazard Ratio (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>IGS(^1)</td>
<td>1.7 (1.0–3.0)</td>
<td>0.01</td>
<td>1.2 (0.7–1.9)</td>
<td>0.004</td>
</tr>
<tr>
<td>Tumor diameter(^2)</td>
<td>1.2 (0.9–1.5)</td>
<td>0.16</td>
<td>1.2 (0.9–1.6)</td>
<td>0.06</td>
</tr>
<tr>
<td>Mastectomy vs. no mastectomy</td>
<td>1.2 (0.8–1.9)</td>
<td>0.40</td>
<td>1.3 (0.9–2.0)</td>
<td>0.21</td>
</tr>
<tr>
<td>Positive estrogen-receptor status vs. negative status</td>
<td>0.5 (0.3–0.8)</td>
<td>0.006</td>
<td>0.9 (0.6–1.3)</td>
<td>0.70</td>
</tr>
<tr>
<td>Tumor grade</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor vs. good differentiation</td>
<td>4.8 (1.4–14.2)</td>
<td>0.005</td>
<td>2.3 (1.1–4.7)</td>
<td>0.03</td>
</tr>
<tr>
<td>Intermediate vs. good differentiation</td>
<td>3.9 (1.3–11.1)</td>
<td>0.01</td>
<td>2.1 (1.0–4.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>Age(^3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive lymph-node status vs. negative status</td>
<td>1.1 (0.3–2.2)</td>
<td>0.84</td>
<td>1.2 (0.7–2.3)</td>
<td>0.49</td>
</tr>
<tr>
<td>No adjuvant therapy vs. chemotherapy or hormonal therapy</td>
<td>1.1 (0.3–2.3)</td>
<td>0.80</td>
<td>1.5 (0.8–2.9)</td>
<td>0.29</td>
</tr>
</tbody>
</table>

\(^a\) The analysis included the 293 patients with breast cancer in the Netherlands Cancer Institute database.

\(^1\) The correlation coefficient for the IGS was modeled as a continuous variable. The hazard ratio is for each increase of 0.1 in the correlation coefficient.

\(^2\) Tumor diameter was modeled as a continuous variable. The hazard ratio is for each increase of 1 cm in diameter.

\(^3\) Age was modeled as a continuous variable. The hazard ratio is for each 10-year increase in age.


---

Risk of Metastasis According to Combined Use of the IGS and Wound Response

Despite < 5% overlap in genes, there was close to 80% concordance in prognostic prediction.

Fan C, et al.,
N Engl J Med
355:560-9, 2006
Prognostic Gene Signatures

- Genes can be combined into multivariable prognostic signatures that do separate outcome groups.

- The confidence intervals around the prognostic risk estimates are still broad
  - For example, 80-95% probability of OS at 10 years.
  - However this is also true for clinical variable based predictors!

- Genomic tests are complementary to clinical variable-based predictions and can refine outcome prediction results within a given clinical group.

Development and Validation of a 21 Gene Assay for N- ER+ Tam+ Patients
(NEJM on line, December 10, 2004)

1. Develop real time RT-PCR method for paraffin block
2. Select candidate genes (N=250)
3. Model building studies (N=447, including 233 from NSABP B-20)
4. Commit to a single 21 gene assay
5. Validation Study in NSABP B-14
### Oncotype DX 21 Gene Recurrence Score (RS) Assay

16 Cancer and 5 Reference Genes From 3 Studies

**PROLIFERATION**
- Ki-67
- STK15
- Survivin
- Cyclin B1
- MYBL2

**ESTROGEN**
- ER
- PR
- Bcl2
- SCUBE2

**INVASION**
- Stromolysin 3
- Cathepsin L2

**HER2**
- GRB7
- HER2

**GSTM1**
- BAG1

**CD68**

**REFERENCE**
- Beta-actin
- GAPDH
- RPLPO
- GUS
- TFRC

<table>
<thead>
<tr>
<th>Category</th>
<th>RS (0 – 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>RS &lt; 18</td>
</tr>
<tr>
<td>Int risk</td>
<td>RS ≥ 18 and &lt; 31</td>
</tr>
<tr>
<td>High risk</td>
<td>RS ≥ 31</td>
</tr>
</tbody>
</table>

Paik S, NEJM 351(27):2817, 2004

---

### Genomic Health-NSABP B-14 Prospective Clinical Validation Study

- **Objective**
  - Validate Recurrence Score as predictor of distant recurrence in N-, ER+, Tamoxifen-treated patients

- **Design**
  - Pre-specified 21 gene assay, algorithm, endpoints, analysis plan
  - Blinded laboratory analysis of three 10 micron tumor block sections

Paik S, NEJM 351(27):2817, 2004
### B-14 Results

#### Distribution of Recurrence Scores (n = 668)

<table>
<thead>
<tr>
<th>Recurrence Score</th>
<th>% of Patients</th>
<th>10-yr Rate Recurrence</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (RS&lt;18)</td>
<td>51%</td>
<td>6.8%</td>
<td>4.0%, 9.6%</td>
</tr>
<tr>
<td>Intermediate (RS 18-30)</td>
<td>22%</td>
<td>14.3%</td>
<td>8.3%, 20.3%</td>
</tr>
<tr>
<td>High (RS≥31)</td>
<td>27%</td>
<td>30.5%</td>
<td>23.6%, 37.4%</td>
</tr>
</tbody>
</table>

Test for the 10-year DRFS comparison between the Low and High risk groups: p<0.00001

Paik S, NEJM 351(27):2817, 2004
### B-14 Results

Cox PH Models for DRFS

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio</th>
<th>95% CI for HR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 50</td>
<td>0.57</td>
<td>(0.39, 0.83)</td>
<td>0.004</td>
</tr>
<tr>
<td>Size &gt; 2.0 cm</td>
<td>1.44</td>
<td>(0.99, 2.11)</td>
<td>0.058</td>
</tr>
<tr>
<td>Age ≥ 50</td>
<td>0.71</td>
<td>(0.48, 1.05)</td>
<td>0.084</td>
</tr>
<tr>
<td>Size &gt; 2.0 cm</td>
<td>1.26</td>
<td>(0.86, 1.85)</td>
<td>0.231</td>
</tr>
<tr>
<td>Recurrence Score</td>
<td>3.21</td>
<td>(2.23, 4.61)</td>
<td>&lt;0.00001</td>
</tr>
</tbody>
</table>

Full model versus reduced model p<0.00001

---

### Recurrence Score as a Continuous Predictor

![Graph showing recurrence score as a continuous predictor](image)

Paik S, et al, SABCS 2003
Recurrence Score as a Continuous Predictor

My RS is 30, What is the chance of recurrence within 10 yrs?

95% CI

B-14 Overall Benefit of Tam
All Patients (N = 645)
By Recurrence Score Risk Category

B-14 Benefit of Tam

Low Risk (RS<18)

Int Risk (RS 18-30)

High Risk (RS ≥31)

Relative risk of tamoxifen for each RS groups in NSABP B-14 (TAM vs placebo)

Low RS≤18

0.551 (0.286-1.059)

Interaction p = 0.06

Inter

0.53 (0.291-0.965)

High RS≥30

0.986 (0.581-1.672)
**Chemotherapy Benefit and Oncotype DX**

NSABP B-20 Chemo Benefit Study in N-, ER+ Pts

**Design**

- Randomized
- Tam + MF
- Tam + CMF
- Tam

Objective: Determine the magnitude of the chemotherapy benefit as a function of 21 gene Recurrence Score assay

**B-20 Results**

- Tam vs Tam + Chemo – All 651 Pts

---

**Graph:**
- DRFS
- N
- Events
- All Patients
- Tam + Chemo: 424, 33
- Tam: 227, 31
- p = 0.02

**Years:**
- 0
- 2
- 4
- 6
- 8
- 10
- 12

**DRFS:**
- 1.0
- 0.9
- 0.8
- 0.7
- 0.6
- 0.5
- 0.4
- 0.3
- 0.2
- 0.1
- 0.0
B-20: Tam alone vs. Tam + Chemotherapy in Node Negative ER+


Low risk (RS<18)

Intermediate risk (RS = 18-30)

High risk (RS≥31)

B20: Relative Risk of Chemotherapy by RS Group

<table>
<thead>
<tr>
<th>RS Group</th>
<th>Relative Risk</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (RS&lt;18)</td>
<td>1.31</td>
<td>(0.46-3.78)</td>
</tr>
<tr>
<td>Inter (RS 18-30)</td>
<td>0.611</td>
<td>(0.24-1.59)</td>
</tr>
<tr>
<td>High (RS≥31)</td>
<td>0.26</td>
<td>(0.13-0.53)</td>
</tr>
</tbody>
</table>

Interaction p = 0.0368
Accomplishments: 21-Gene Recurrence Score is Predictive of CAF Chemotherapy Benefit in Postmenopausal, N+, ER+ Breast Cancer

TBCT 0100 (SWOG 8814)

RANDOMIZE

n = 1477

- tamoxifen x 5 yrs
  (n = 361)
- CAF x 6, then concurrent tam
  (n = 566)
- CAF x 6, then tamoxifen
  (n = 550)

Used for Correlative Science Studies

n = 148

Prognosis in Tam ONLY by RS

Disease-Free Survival by Risk Group
(tamoxifen alone)

Stratified log-rank p = 0.017 at 10 years

Low RS <18 (n=55)
Intermediate RS 18-30 (n=46)
High RS ≥31 (n=47)

S8814: Little or NO CAF Benefit in Low RS; Increases with Higher RS

Low
(RS <18)

Intermediate
(RS 18-30)

High
(RS ≥31)

- Tam only
  (n=47, 26 events)
  Tamoxifen
  (n=46, 22 events)
- CAF-Tam
  (n=57, 20 events)
- CAF-Tam
  (n=56, 26 events)

Stratified log-rank p = 0.033 at 10 years

Stratified log-rank p = 0.48 at 10 years

Stratified log-rank p = 0.97 at 10 years

Stratified log-rank p = 0.033 at 10 years

Similar Effect Seen Regardless of Number of Involved Axillary Lymph Nodes

n = 367

Albain, et al. PSABCS 2007; Manuscript under review by Lancet
Intergroup - PACCT trial

Node Negative ER +

Oncotype DX Assay

LOW Risk
Hormone Therapy Registry

Intermediate Risk
Randomize Hormone Rx vs. Chemotherapy + Hormone Rx

HIGH Risk
Chemotherapy + Hormone Rx

Evaluate Clinical-Pathological risk and 70-gene signature risk

<table>
<thead>
<tr>
<th>Discordant</th>
<th>50%</th>
<th>50%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clin-Path HIGH</td>
<td>N=1680</td>
<td></td>
</tr>
<tr>
<td>70-gene LOW</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>Clin-Path LOW</td>
<td>N=420</td>
<td></td>
</tr>
<tr>
<td>70-gene HIGH</td>
<td>20%</td>
<td></td>
</tr>
</tbody>
</table>

N=6000
ER absent

Chemotherapy 4350 patients

Endocrine therapy 6000 patients

R1

R2

Anthracycline based
Taxane
Capetabine based

R3

2 yrs Tam 
5 yrs Letrozole
7 yrs Letrozole
MDACC 200-gene Endocrine Sensitivity Index

Hypothesis: Genes that are highly co-expressed with ER may be a summary measure of ER activity and correlate with benefit from endocrine therapy.

Discovery set, N=286 (77 ER-, 209 ER+)

Define 200 most highly ER-associated genes

Combine these into a 200-gene ER activity index (does not include ER itself!)

Test the predictive value on independent cases

Association between ER-gene Index and Relapse in ER-positive Patients treated with 5-years of Tamoxifen (Validation set, n=277, Institut Jules Bordet)

Distant Relapse Free Survival (DRFS) at 5 years

The ER activity index (SET) is a strong predictor of survival after Tamoxifen adjuvant therapy.

WF Symmans et al (SABCS, 2006 (Abst #1027))
ER status can be determined by measuring ER mRNA levels.

A separate 200-gene signature can identify among the ER-positive patients those who have excellent survival with 5-years of endocrine therapy.
Chemotherapy Response Prediction
Predictor discovery and validation strategy for Paclitaxel/FAC neoadjuvant chemotherapy

**DISCOVERY PHASE**
Pretreatment FNA (n=82) → Affymetrix U133A profiling → Preoperative Paclitaxel / FAC → differentially expressed genes

Pathologic CR (26%) → Residual cancer (74%)

Combine genes into multivariable prediction model

**VALIDATION PHASE**
Pretreatment FNA (n=51, independent cases) → Affymetrix U133A profiling → Preoperative Paclitaxel / FAC → Compare predicted versus observed response

**Comparison of the 30-gene Pharmacogenomic Predictor with a Multivariable Clinical Predictor**

<table>
<thead>
<tr>
<th></th>
<th>Clinical variables</th>
<th>DLDA-30 probe sets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accuracy</td>
<td>0.78 (0.65-0.89)</td>
<td>0.76 (0.62-0.87)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.61 (0.32-0.86)</td>
<td>0.92 (0.64-1.0)</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.84 (0.69-0.94)</td>
<td>0.71 (0.54-0.85)</td>
</tr>
<tr>
<td>PPV</td>
<td>0.57 (0.29-0.82)</td>
<td>0.52 (0.3-0.7)</td>
</tr>
<tr>
<td>NPV</td>
<td>0.86 (0.71-0.95)</td>
<td>0.96 (0.82-1.0)</td>
</tr>
</tbody>
</table>

Genomic test (AUC=0.87)
Clinical variables only (age, grade, ER) (AUC=0.81)


Multiagent Chemotherapy Response

<table>
<thead>
<tr>
<th>Subtype</th>
<th>NSABP B-27</th>
<th>ISPY</th>
<th>Hess et al</th>
<th>All Studies</th>
<th>Overall Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luminal A</td>
<td>0/25 (0%)</td>
<td>2/39 (5%)</td>
<td>0/36 (0%)</td>
<td>2/101 (2%)</td>
<td>27%</td>
</tr>
<tr>
<td>Luminal B</td>
<td>1/7 (13%)</td>
<td>4/26 (13%)</td>
<td>5/22 (19%)</td>
<td>10/55 (15%)</td>
<td>17%</td>
</tr>
<tr>
<td>Her2-enriched</td>
<td>1/10 (9%)</td>
<td>12/10 (55%)</td>
<td>12/17 (41%)</td>
<td>25/37 (40%)</td>
<td>16%</td>
</tr>
<tr>
<td>Basal-like</td>
<td>13/41 (24%)</td>
<td>15/29 (34%)</td>
<td>16/11 (59%)</td>
<td>44/81 (55%)</td>
<td>33%</td>
</tr>
<tr>
<td>Normal-like</td>
<td>3/1 (75%)</td>
<td>3/3 (50%)</td>
<td>1/13 (7%)</td>
<td>7/17 (29%)</td>
<td>6%</td>
</tr>
<tr>
<td>All Subjects</td>
<td>18/85 (17%)</td>
<td>36/167 (25%)</td>
<td>34/99 (26%)</td>
<td>88/291 (29%)</td>
<td>29%</td>
</tr>
</tbody>
</table>

Different multiagent regimens
- NSABP B-27: AC or AC/T
- Hess et al: T/FAC
- ISPY:

Hess et al., JCO 2006
Beat et al., JCO 2003

2nd Generation T/FAC Response Predictor
(HER2 normal, ER-stratified)

T/FAC Cases N=274

Non-Usable Cases
(failed QC, no path review, no RCB)
N=12

T/FAC Cases Available N=262

HER2 Normal N=229

pCR: 21.4% (56)
RCB-0/I: 32.1% (84)
RCB-III: 25.3% (58)

HER2 Positive N=23

pCR: 39.4% (13)
RCB-0/I: 46.4% (15)
RCB-III: 15.2% (3)

ER Positive N=132

pCR: 36.1% (43)
RCB-0/I: 47.4% (46)
RCB-III: 23.7% (23)

ER Negative N=97

C Hatzis, WF Symmans, L Pusztai
Accuracy in 3-fold Cross Validation

ER-, HER2 normal breast cancer, if positive for test 7 x higher probability of pCR or near pCR compared to test negative cases

ER+, HER2 normal breast cancer, if positive for test 5 x higher probability of pCR or near pCR compared to test negative cases

Clinical Development Stages of Genomic Diagnostic Tests for Breast Cancer

Discovery Marker optimization

Independent validation of accuracy

Prove clinical utility

PROGNOSTIC TESTS:
- 70-gene prognostic signature
- 21-gene recurrence score
- 76-gene prognostic signature
- "molecular classification"

PREDICTIVE TESTS:
- 44-gene Tamoxifen predictor
- 57-gene EC predictor
- 92-gene Docetaxel predictor
- 85-gene Docetaxel predictor
- MDACC Taxol/FAC predictor
- MDACC 2003-0321
- 200-gene SET predictor
- JBI data set

Andre F and Pusztai L (2006)
Where do Breast Cancer Related Genomic Tests Stand Today?

- MammaPrint, Oncotype DX, and the 70-gene prognostic signature are validated tests with imperfect but reasonably well understood performance characteristics.
  - Oncotype Dx is commercially available and reimbursed in the USA
  - MammaPrint was cleared by the US FDA as adjunct to existing clinical prognostic variables

- A second tier of similar and complementary genomic tests were also developed that still await independent validation.

Can (the current best) Genomic Tests Improve Clinical Outcome in Breast Cancer?

There are many shades of “improved clinical outcome”

- Improved survival
  - Depends on competing treatment strategies
    - ? TAILOR Rx

- Same survival less toxicity
  - Depends on test accuracy (and toxicity)
    - ? MINDACT

- Same survival less cost
  - Depends on how MDs use the test
    - ✓ Oncotype DX

- Improved satisfaction with treatment decision
  - Help make a decision when “on the fence”
    - ✓ Oncotype DX
The better the prognostic and predictive information is, the more appropriate the treatment decision will be for a particular individual.
Hierarchical Clustering and SigClust Analysis of Microarray Data using 1,906 "intrinsic" Genes and 189 Samples

PAM50 Intrinsic Subtype Prognosis for Relapse-free Survival (RFS)

Risk of Relapse (ROR) Predictions using a Test Set of Node-negative, No Systemic Therapy Patients
Analysis of an Old-aged Formalin-fixed, Paraffin-embedded Patient Cohort


Relationship between Risk of Relapse (ROR) Score and Paclitaxel, Fluorouracil, Doxorubicin, and Cyclophosphamide Neoadjuvant Response

Conclusions

- There are multiple validated prognostic indicators for breast cancer. These are largely useful for predicting outcome for groups of patients
- Adjuvant!online is arguably the current, most useful clinical prognostic model, including estimation of treatment benefit
- Several genomic prognostic models appear to have similar prognostic efficacy; at least one has been suggested to be superior to Adjuvant!online
- The clinical utility of individual genomic models and combinations of clinical and genomic prognostic models is currently under evaluation
Final Conclusions

• Imperfect predictive tests still could provide value when integrated with other sources of information.

• Combination of individually weak tests might be successfully assembled into successful diagnostic strategies (think of imaging modalities).

• Not all patients may require a novel prognostic or predictive test, but for some these tests can lead to better medical decision making.

“Perfection is the enemy of the good.”
Gustave Flaubert,
French novelist (1821 - 1880)