WHERE ARE WE NOW, TO THE PRECISION MEDICINE

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COI: Research grant; Chugai, Taiho
Estimated Cancer Incidence and Mortality 2015

National Cancer Center: ganjoho.jp  28/04/2015

Incidence

Mortality

Site
-- Stomach
-- Colorectal
-- Lung
-- Prostate
-- Breast
-- Liver
-- Pancreas
Precision Medicine

• Prediction of Disease Course
• Characterization and Monitoring of Primary and Metastatic Tumors
• Individualized Care
BOADICEA Mutation Carrier Possibilities

(a) Unknown Family History as a Function of Her Breast Cancer Diagnosis Age

(b) Who was Diagnosed with Breast Cancer at Age 30 and Whose Mother was Diagnosed with Breast Cancer, as a Function of Her Mother’s age at Diagnosis

BOADICEA Breast Cancer Risk
Oncotype DX® Distant BC Free Survival
ER+/HER2-, n0, Age 40-84y.o.
Hormone therapy+

Chemotherapy
69% of RS ≥31
34% of RS 18-30
7% of RS <18

Petkov et al, npj Breast Cancer, 2016
### Cox Proportional Hazards Model

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Parameter Estimate</th>
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<tbody>
<tr>
<td>Age at random assignment, years</td>
<td></td>
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<tr>
<td>&lt; 35</td>
<td>0.81</td>
</tr>
<tr>
<td>35-39</td>
<td>0.54</td>
</tr>
<tr>
<td>40-44</td>
<td>0.23</td>
</tr>
<tr>
<td>45-49</td>
<td>0 (ref)</td>
</tr>
<tr>
<td>≥ 50</td>
<td>0.16</td>
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<tr>
<td>No. of positive nodes</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0 (ref)</td>
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<tr>
<td>1-3</td>
<td>0.38</td>
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<tr>
<td>≥ 4</td>
<td>1.12</td>
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<tr>
<td>Tumor size, cm</td>
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<tr>
<td>Unknown</td>
<td>0.61</td>
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<tr>
<td>≤ 2</td>
<td>0 (ref)</td>
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<tr>
<td>&gt; 2</td>
<td>0.42</td>
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<tr>
<td>ER expression, %</td>
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<td>-0.10</td>
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<tr>
<td>&lt; 50</td>
<td>0.23</td>
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<tr>
<td>≥ 50</td>
<td>0 (ref)</td>
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<tr>
<td>PgR expression, %</td>
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<td>0.95</td>
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<tr>
<td>≥ 20</td>
<td>0.27</td>
</tr>
<tr>
<td>≥ 50</td>
<td>0 (ref)</td>
</tr>
<tr>
<td>Tumor grade</td>
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</tr>
<tr>
<td>1</td>
<td>0 (ref)</td>
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<tr>
<td>2</td>
<td>0.83</td>
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<tr>
<td>3</td>
<td>1.10</td>
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<td>Ki-67 expression, %</td>
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<tr>
<td>&lt; 14</td>
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<td>14-19</td>
<td>0.07</td>
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<tr>
<td>≥ 14</td>
<td>0.29</td>
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<tr>
<td>≥ 26</td>
<td>0.45</td>
</tr>
</tbody>
</table>

### Composite Measure of Risk

**No Chemotherapy**
- 1353 cases (SOFT)

**+ Chemotherapy**
- 1271 cases (SOFT)

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St. Gallen 2017

Escalating & De-Escalating of Treatment

ER+/ HER2- Luminal type

Clinico-Pathological Multigene

Chemotherapy
Hormone Therapy:
Combo. and/or Extended

No Chemotherapy,
TAM alone
A Real Case

- 55 y.o
- 2.5cm
- One node involved
- ER-high/ HER2-/ PgR-low/ Ki67 LI 35%
- Grade 3
- AC-T
- Aromatase inhibitor
- Distant Recurrences (DFI: 2.6 year)
Subclonal architecture of Metastatic Breast Cancer (Luminal)

HER2 expression identifies dynamic functional states within circulating breast cancer cells

Nicole Vincent Jordan¹, Aditya Bardia¹,², Ben S. Wittner¹,², Cyril Benez³, Matthew Ligorio¹,³, Yu Zhong¹, Min Yu¹,², Tilak K. Sundaresan¹,², Joseph A. Liaus³, Rushil Desai¹, Ryan M. O’Keefe¹, Richard Y. Ebright¹, Myriam Boukall¹, Srinjoy Sill¹, Maristela L. Onozato¹,⁴, Anthony J. Iafrate¹,⁴, Ravi Kapur⁵, Dennis Sgroi¹,⁶, David T. Ting¹,², Mehmet Tone⁴,⁵, Sridhar Ramaswamy¹,², Wilhelm Haas¹,², Shyamala Maheswaran¹,³,⁴†, and Daniel A. Habor¹,²,⁶,⁴†

¹Massachusetts General Hospital Cancer Center, Harvard Medical School, Charlestown, MA
Risk-driven: Stage, Biomarker and Response

Stage
Pathology
Multi-gene
Biomarker

Low-risk
Local therapy
De-escalated Systemic Therapy

High-Risk
Escalated Systemic therapy

Residual Invasive Disease+
Metastatic Disease+ (node, CTC..)

Favorable
Standard

Unfavorable
New Therapy
Clinical Trials

- Non HER2: Capecitabine
- ER+/HER2- (High Risk): TS-1, Palbociclib
- gBRCAmt: Olaparib
- HER2+: TDM-1
- TNBC: PD-1
OlympiA and OlympiAD: randomized Phase III trials of olaparib in patients with breast cancer and a germline BRCA1/2 mutation

- TNBC
- HR+, HER2-, Extensive n+
- gBRCA1/2 mutation
- Completed adequate surgery
- Completed at least 6 cycles chemotherapy neoadjuvant or adjuvant

Presented at ESMO, Madrid, Spain, 26–30 September 2014
PD-1/PD-L1
If **favorable** prognosis is predicted precisely

- Minimal Surgery
Local Therapy

Treatment of low-risk ductal carcinoma in situ: is nothing better than something?
De-escalation of axillary surgery in early breast cancer

Ismail Jatoi, John R Benson, Masakazu Toi

Oct 2016
Volume 17
Number 10
p1335-1462 e415-e467
If favorable prognosis is predicted precisely

- Minimal Surgery
- Low risk ER+/HER2-: Positive
- Early stage HER2+: TDM1
Anti-HER2 NEO: JBCRG-20 (Neo-peaks)

A
N=50
TCbH→ Per
MRI
N=200
TCb-H+PER

B
N=50
TCbH→ Per
MRI
ER(+):Hormone
TDM1+PER

C
N=100
TDM1→ Per
MRI
ER(+):Hormone
Responder
TDM1+PER→ Cont. or FEC

Non-Responder
FEC
FEC
FEC
FEC
FEC

CpCR: Pathological complete response + node-negative
Dedicated Breast PET System
Phantom Comparison
(mini Derenzo phantom for small animal PET)

1.6mm is clearly seen

Elmammo

PET
Case 1 (Breast dedicated PET)

Case 2

Molecular Imaging PET

64Cu-DOTAtрастузумаб PET images

RISK
Systemic Therapy Burden, Intensity
Therapeutic Efficacy
Toxicity
Cost
THANK YOU

Acknowledgements
BIG/GBG, JBCRG, Shimadzu
Radiology, Radiation Oncology,
Breast Cancer Unit, Kyoto University
BOADICEA Breast Cancer Risk by Mutation Status and Family History

Family History unknown

Her Mother Breast Cancer at her 40 y.o.

BOADICEA Breast Cancer Risk
IBCSG SOFT TEXT study

A

Age

B

n

C

T

D

ER

Trastuzumab Emtansine versus Trastuzumab as Adjuvant therapy in patients with HER2-positive breast cancer who have Residual Tumor following Preoperative Therapy (Phase 3: KATHERINE, NCT01772472)

- T1-4/N0-3/M0 at presentation
- Completion of at least 6 cycles of chemotherapy (at least 16 wks), including at least 9 wks of trastuzumab and at least 9 wks of taxane-based therapy
- Invasive disease-free survival (IDFS)