Elderly Breast Cancer – Systemic Therapy

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Founding Convenor
Hong Kong Breast Oncology Group
Scientific Committee Meeting
International Society of Geriatric Oncology (SIOG 2017)

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Disclosures

Consultant or Advisory Role:

AstraZeneca, Aptus, Astellas, Eisai, GlaxoSmithKline, Foundation Medicine, Novartis & Pfizer

Due to time constraint, I will just be focusing on systemic therapy for EBC patients!
Outline

- The undeniable emerging needs
- Current Dilemmas for Elderly BC patients
- Opportunities & Challenges
- Conclusion
Outline

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Age is a known risk factor...

• **AGE** is one of the strongest risk factors for cancer development

• The aging population presents a major epidemiological challenge
  
  – Demographic shift brought by the baby-boomer generation

14th International Society of Geriatric Oncology, Lisbon, October, 2014
By 2030, there could be 50% more people greater than 65 years old, and 100% more people greater than 80 years old.

By the year 2030, most patients with cancer will be aged over 65 years and many will be frail.

Aging Society & Aging Cancer Patients

Age and Cancer Trends: A 20-year review of the Hong Kong Cancer Registry

Cancer Incidence for 65 years old or above (1991-2011)

VSM Lam, ST Yung, OWK Mang, RK Ngan, J Tsang HKICC 2014
Distribution of Female Breast Cancer by Age Group & Type in 2011

**Distribution of Female Breast Cancer by Age Group and Type (Invasive and Ca in-situ) in 2011**

1. **Invasive BC aged >=65:**
   - 818/3419 = 23.9%

2. **Invasive BC aged >=75:**
   - 423/3419 = 12.37%

1 in 4 65 y.o. or above

1 in 8 75 y.o. or above

Source: Hong Kong Cancer Registry, Hospital Authority

Yearly incidence rates of Female Breast Cancer (per 100,000 women) by Type (Invasive and Ca in-situ) in 2011

**Lifetime risk**
- 1 in 17
- 1 in 112
- 1 in 15

**Crude rate**
- 90.7
- 12.8
- 103.6

**ASR (World)**
- 61.0
- 8.8
- 69.9

**1 in 4 65 y.o. or above**

**年齡超過65歲之乳腺癌患者:**
Invasive BC aged >=65: 818/3419 = 23.9%

**年齡超過75歲之乳腺癌患者:**
Invasive BC aged >= 75: 423/3419 = 12.37%
Elderly cancer patients are different...

• Age-related reduced organ functions
• Multiple co-morbidities
• Changes in cognition
  – Dementia, delirium
  – 1% in 65-69 y.o., 41% in >90 y.o. having dementia
• Falls
• Poly-pharmacy
• Higher prevalence of depression & anxiety
Elderly cancer patients are different...

• Different cancer types
  – Marked increase in epithelial carcinomas from 40 to 80 y.o.
  – Cancer & aging share common etiologies – genomic instability & reduced rate of autophagy
  – Breast Cancer among elderly are mostly hormone positive with slow tempo of disease.
Impact of Aging on treatment decision making...

- Surgery – definitive vs palliative
  - Surgical and anaesthetic risk
- Radiotherapy – tolerance and toxicities
  - Poor nutrition or malnourished, cachexia
- Chemotherapy
  - Dose adjustment, dose reduction, tailored regimen
- Hormonal therapy
- Targeted therapy
Outline

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- Conclusion
Misconception...
about Elderly Cancer Patients

• “Chronological age used to be the sole important determining factor driving the aging process”

• “Chronological age is the common reference to decide treatment plan for elderly cancer patients”

• “Elderly cancer patients do not tolerate chemotherapy or any anticancer agent easily”

• “There is much toxicities related to elderly with multiple comorbidities...”
Current Dilemmas

1) Therapeutic **nihilism**
   - Elderly patients do not receive any treatment

2) The **intermediate** position?
   • –Elderly patients may benefit from treatments

3) Blind therapeutic **enthusiasm**
   - Elderly patients receive **futile/non-beneficial treatments**
Current Dilemmas

1) Therapeutic nihilism
   - Elderly patients do not receive any treatment

2) The intermediate position?
   • Elderly patients may benefit from treatments

3) Blind therapeutic enthusiasm
   - Elderly patients receive futile/non-beneficial treatments

Under-treatment vs Over-treatment...
Almost all age-related changes lead to reduced organ function.

There are 3 different trajectories of aging:
- Aging with pathology & disability
- Normal aging with some disability
- Successful aging with minimal disability

Aging is a heterogeneous process...
BC biology according to age

de Kruijf Mol Oncol 2014, Jenskins Oncologist 2014
Undertreatment

SEER database; 49,616 women with stage I/II breast cancer ≥67y

Initial treatment for stage II breast cancer by age

Treated with chemotherapy if ER+ N+ stage I/II breast cancer

BCS = breast conserving surgery; XRT = radiotherapy

Schonberg JCO 2010
Undertreatment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HR of Death Due to Breast Cancer</th>
<th>Range</th>
<th>HR of Death Due to Other Causes</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>67-69</td>
<td>1.0</td>
<td>0.9-1.2</td>
<td>1.3</td>
<td>1.2-1.4</td>
</tr>
<tr>
<td>70-74</td>
<td>1.1</td>
<td>0.99-1.3</td>
<td>1.6</td>
<td>1.6-2.2</td>
</tr>
<tr>
<td>75-79</td>
<td>1.2</td>
<td>1.1-1.4</td>
<td>3.0</td>
<td>2.7-3.3</td>
</tr>
<tr>
<td>80-84</td>
<td>1.5</td>
<td>1.3-1.7</td>
<td>4.1</td>
<td>3.7-4.6</td>
</tr>
<tr>
<td>≥ 85</td>
<td>1.8</td>
<td>1.5-2.2</td>
<td>5.9</td>
<td>5.2-6.7</td>
</tr>
</tbody>
</table>

Substudy from TEAM trial (adjuvant exemestane)

<table>
<thead>
<tr>
<th>Cause specific death</th>
<th>Age &lt;65y</th>
<th>Age 65 – 74y</th>
<th>Age ≥75y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other cause mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Univariate HR 1.66
  (95% CI 1.34-2.08), p<0.001
- Multivariable HR 1.63
  (95% CI 1.23-2.16), p<0.001

Schonberg JCO 2010, Van de Water JAMA 2012
Overtreatment

- A sizeable proportion of elderly with operable breast cancer die of NON-CANCER-related causes

<table>
<thead>
<tr>
<th>Age</th>
<th>Total deaths</th>
<th>Deaths from breast cancer</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>50–69</td>
<td>1334</td>
<td>933</td>
<td>70</td>
</tr>
<tr>
<td>70–74</td>
<td>514</td>
<td>293</td>
<td>57</td>
</tr>
<tr>
<td>75–79</td>
<td>696</td>
<td>329</td>
<td>47</td>
</tr>
<tr>
<td>≥ 80</td>
<td>1681</td>
<td>663</td>
<td>39</td>
</tr>
<tr>
<td>Total</td>
<td>4225</td>
<td>2218</td>
<td>53</td>
</tr>
</tbody>
</table>

53% of elderly BC patients aged 75-79 and 61% elderly patients aged >= 80 died of other non-BC causes

- Absolute benefit of treatments is lower

Ali Br J Cancer 2011
Adjuvant chemo

DFS

All

≤50

OS

All

≤50

51-64

≥65

Results

- Benefit identical
- Toxicity careful!!

- Toxic deaths 1.5%

CALGB (1975-1999)

4 randomized trials

6487 pts

> 65 yo 542 (8%)

> 70 yo 159 (2%)

Muss JAMA 2005
## Adjuvant chemotherapy and mortality

<table>
<thead>
<tr>
<th></th>
<th>Giordano*</th>
<th></th>
<th>Elkin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I-III, ∀ ER , 65+</td>
<td>I-III, ER-, 66+</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No. total</td>
<td>41,390</td>
<td>5,081</td>
</tr>
<tr>
<td></td>
<td>No. w/CT</td>
<td>4,500</td>
<td>1,711</td>
</tr>
<tr>
<td>pN</td>
<td>ER</td>
<td>HR (95% IC)</td>
<td>HR (95% IC)</td>
</tr>
<tr>
<td>pN0</td>
<td>∀</td>
<td>1.05 (0.85-1.31)</td>
<td>NA</td>
</tr>
<tr>
<td>pN+</td>
<td>+</td>
<td>1.05 (0.85-1.31)</td>
<td>NA</td>
</tr>
<tr>
<td>both</td>
<td>-</td>
<td>NA</td>
<td>0.85 (0.77-0.95)</td>
</tr>
<tr>
<td>pN+</td>
<td>-</td>
<td>0.72 (0.54-0.96)</td>
<td>0.76 (0.65-0.88)</td>
</tr>
<tr>
<td>pN+ &gt; 70 yo</td>
<td>-</td>
<td>0.74 (0.56-0.97)</td>
<td></td>
</tr>
</tbody>
</table>

*: BC specific mortality

Adjuvant chemo is useful FIRST in ER-, pN0 or pN+, even > 70 yo

Giordano & Elkin J Clin Oncol 2006
Milestones of HER2/anti-HER2 therapies in BC

- **1978**: EGFR discovery (Cohen)
- **1978**: Her2/neu oncogene discovery (Weinberg)
- **1982**: EGFR MoAb inhibited growth (Mendelsohn)
- **1983**: Her2 cloned (Ullrich and Coussens)
- **1984**: Her2 amplification in breast cancer (Aaronsen)
- **1985**: Her2/neu amplification correlates with shorter survival (Slamon)
- **1987**: FDA approves trastuzumab alone for 2nd line and in with paclitaxel for 1st line MBC
- **1987**: Her2/neu amplification correlates with shorter survival (Slamon)
- **1998**: FDA approves trastuzumab in adjuvant setting
- **2006**: FDA approves lapatinib + letrozole for MBC
- **2007**: FDA approves trastuzumab + capecitabine for MBC
- **2007**: FDA approves trastuzumab + docetaxel for MBC
- **2010**: FDA approves pertuzumab + trastuzumab + docetaxel for MBC
- **2012**: FDA approves trastuzumab emtansine (TDM-1) for MBC
- **2013**: Accelerated approval of pertuzumab/trastuzumab as neoadjuvant therapy

**MBC**: metastatic breast cancer; **MoAb**: monoclonal antibody
# DFS & OS w/ trastuzumab 1 year

<table>
<thead>
<tr>
<th>Study</th>
<th>Follow-up (years)</th>
<th>DFS</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>HR</td>
<td>p value</td>
</tr>
<tr>
<td>HERA¹⁻⁴ CT+/–RT→H vs. CT+/–RT</td>
<td>1</td>
<td>3387</td>
<td>0.54</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>3401</td>
<td>0.64</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>3401</td>
<td>0.76</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>3401</td>
<td>0.76</td>
</tr>
<tr>
<td>NCCTG N9831/NSABP B-31⁵⁻⁷ AC→TH→H vs. AC→T</td>
<td>2</td>
<td>3351</td>
<td>0.48</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>4045</td>
<td>0.52</td>
</tr>
<tr>
<td></td>
<td>8.4</td>
<td>4046</td>
<td>0.60</td>
</tr>
<tr>
<td>BCIRG 006⁸</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AC→TH→H vs. AC→T</td>
<td>5.5</td>
<td>3222</td>
<td>0.64</td>
</tr>
<tr>
<td>TCH vs. AC→T</td>
<td></td>
<td></td>
<td>0.75</td>
</tr>
</tbody>
</table>

**AMM FDA/EMA 2006**

CT, chemotherapy; DFS, disease-free survival; H, trastuzumab; HR, hazard ratio; OS, overall survival; RT, radiotherapy; T, taxane.

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Trastuzumab adjuvant & DFS

<table>
<thead>
<tr>
<th>Study</th>
<th>HR all</th>
<th>(95%CI)</th>
<th>HR 60+</th>
<th>(95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HERA</td>
<td>0.64</td>
<td>0.54-0.76</td>
<td>0.91</td>
<td>0.59-1.41</td>
</tr>
<tr>
<td>NSABP-B31/N9831</td>
<td>0.48</td>
<td>0.39-0.59</td>
<td>0.41</td>
<td>0.24-0.68</td>
</tr>
<tr>
<td>BCIRG 006</td>
<td>0.61</td>
<td>0.37-0.65</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>FinHER</td>
<td>0.42</td>
<td>0.21-0.83</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>PACS-04</td>
<td>0.86</td>
<td>0.61-1.22</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

> 60 yo ≤ 16% in HERA for ex!
Elders with Breast Cancer Tend to Delay Seeking Medical Care and Present with a Later Cancer Stage

Janice Tsang, Polly Cheung, Hang-mei Lee, Gary Tse, Sam Choy, Lorna Wong, Maria Shiu, Thomas Yau, Chun-Chung Yau

Steering Committee
Hong Kong Breast Cancer Registry
Hong Kong Breast Cancer Foundation

3rd March, 2017

Symposium on Elderly Primary Breast Cancer Women
East Midlands Conference Centre, Nottingham
Subjects and Methodology

• 13,265 female patients with breast cancer, diagnosed between 2006 and 2015, from the Hong Kong Breast Cancer Registry were studied. Among them, 861 patients were aged 70 years or above.

• Chi square test was used to test for any significant differences between the elderly patients and patients of all ages in the following areas:
  – How the breast cancer was first detected
  – Tumour characteristics
  – Types of treatment

• Comorbidity of elderly patients were also assessed by using the Charlson Comorbidity Index (CCI)
# Elderly patients received more mastectomies & less chemotherapy and radiotherapy

<table>
<thead>
<tr>
<th></th>
<th>≥70 yo patients</th>
<th>Patients of all ages</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>N (%)</td>
<td></td>
</tr>
<tr>
<td><strong>Surgery</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>40 (5)</td>
<td>186 (2)</td>
<td></td>
</tr>
<tr>
<td>Breast-conserving surgery (BCS)</td>
<td>91 (12)</td>
<td>3,785 (33)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Mastectomy (MTX)</td>
<td>608 (82)</td>
<td>6,562 (57)</td>
<td></td>
</tr>
<tr>
<td><strong>Chemotherapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>8 (3)</td>
<td>1,544 (39)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>II</td>
<td>30 (10)</td>
<td>4,035 (84)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>III</td>
<td>32 (33)</td>
<td>1,574 (94)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>IV</td>
<td>11 (42)</td>
<td>259 (87)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Targeted therapy</td>
<td>15 (14)</td>
<td>1,146 (55)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Endocrine therapy</td>
<td>576 (79)</td>
<td>8,605 (76)</td>
<td>0.098</td>
</tr>
<tr>
<td><strong>Radiotherapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Among patients with BCS</td>
<td>80 (91)</td>
<td>3,591 (97)</td>
<td>0.010*</td>
</tr>
<tr>
<td>Among patients with MTX</td>
<td>198 (33)</td>
<td>3,654 (50)</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

*p<0.05 indicates significant difference
Elderly patients with higher CCI received more conservative treatment

<table>
<thead>
<tr>
<th></th>
<th>CCI =0 N (%)</th>
<th>CCI =1-2 N (%)</th>
<th>CCI ≥3 N (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>48 (8)</td>
<td>8 (5)</td>
<td>11 (30)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>6 (4)</td>
<td>1 (2)</td>
<td>1 (25)</td>
<td>N/A</td>
</tr>
<tr>
<td>II</td>
<td>25 (10)</td>
<td>4 (7)</td>
<td>0 (0)</td>
<td>N/A</td>
</tr>
<tr>
<td>III</td>
<td>25 (34)</td>
<td>8 (38)</td>
<td>0 (0)</td>
<td>N/A</td>
</tr>
<tr>
<td>IV</td>
<td>--</td>
<td>--</td>
<td>10 (40)</td>
<td>N/A</td>
</tr>
<tr>
<td>Targeted therapy</td>
<td>12 (16)</td>
<td>3 (13)</td>
<td>0 (0)</td>
<td>N/A</td>
</tr>
<tr>
<td>Endocrine therapy</td>
<td>464 (75)</td>
<td>120 (77)</td>
<td>27 (77)</td>
<td>0.740</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Among patients with BCS</td>
<td>81 (88)</td>
<td>15 (88)</td>
<td>3 (60)</td>
<td>N/A</td>
</tr>
<tr>
<td>Among patients with MTX</td>
<td>146 (31)</td>
<td>42 (33)</td>
<td>9 (45)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*p<0.05 indicates significant difference
Outline

- The undeniable emerging needs
- Current Dilemmas for Elderly BC patients
- Opportunities & Challenges
- Conclusion
Changing Portraits of Breast Cancer over the past decades...
The top research priority found was “the identification of molecular signatures to select patients who could be spared from chemotherapy. The second most pressing issue also involved chemotherapy, namely the identification of features to help clinicians choose the most optimal chemotherapy regimen for individual patients.”
Standard decision tools

- **Adjuvant! Online**
- **Predict**

Tumor extent:
- T (tumor size)
- N (nodal status)

Tumor biology
- Luminal A
- Luminal B HER2 neg
- Triple negative Her2+

**Therapy choice depends on ...**

Patient preference

General health status:
- Geriatric assessment
  - Estimate life-expectancy
  - Predict treatment toxicity

not accurate in older patients
quite accurate for OS prediction

De Glas Lancet Oncol 2014 & Br J Cancer 2016
Early 2000s: 1st GEP (intrinsic classification)

- Quantification of mRNA or cDNA of genes involved in tumour proliferation
- To identify patients requiring chemo despite good standard prognostic factors
- To avoid chemo in others
- Better individual risk stratification

Prat Mol Oncol 2011
Various options of molecular genomic profiling tools...

<table>
<thead>
<tr>
<th>Provider</th>
<th>MammaPrint</th>
<th>Oncotype DX</th>
<th>Breast Cancer Index</th>
<th>Mapquant DX</th>
<th>PAM 50 ROR</th>
<th>EndoPredict</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Assay</td>
<td>70-gene assay</td>
<td>21-gene recurrence score</td>
<td>2-gene ratio (H/I) and molecular grade index</td>
<td>Genomic grade</td>
<td>50-gene assay</td>
<td>12-gene assay</td>
</tr>
<tr>
<td>Type of Sample</td>
<td>Fresh or frozen or FFPE</td>
<td>FFPE</td>
<td>FFPE</td>
<td>Fresh or frozen or FFPE</td>
<td>FFPE</td>
<td>FFPE</td>
</tr>
<tr>
<td>Technique</td>
<td>DNA microarray or qRT-PCR</td>
<td>qRT-PCR</td>
<td>qRT-PCR</td>
<td>DNA microarray or qRT-PCR</td>
<td>qRT-PCR</td>
<td>qRT-PCR</td>
</tr>
<tr>
<td>Clinical Application</td>
<td>Prognosis of NO, &lt; 5 cm, stage I/II, age &lt; 61</td>
<td>Prediction of recurrence risk in ER+ and N0 treated with TAM</td>
<td>Prognostic in ER+, prediction of response to TAM</td>
<td>Molecular grading for ER+, histologic grade II disease</td>
<td>Originally for intrinsic subtyping, recurrence prediction</td>
<td>Recurrence prediction for ER+ HER2+</td>
</tr>
<tr>
<td>Results Presentation</td>
<td>Dichotomous, good or poor prognosis</td>
<td>Continuous variable</td>
<td>Continuous variable</td>
<td>Dichotomous, GGI I or GGI III</td>
<td>Continuous variable</td>
<td>Dichotomous, low or high risk</td>
</tr>
<tr>
<td>Level of Evidence</td>
<td>I</td>
<td>I</td>
<td>III</td>
<td>III</td>
<td>I</td>
<td>I</td>
</tr>
<tr>
<td>FDA Approval</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>NO</td>
<td>YES</td>
</tr>
</tbody>
</table>

Abbreviations: ER+, estrogen receptor-positive; FFPE, formalin-fixed, paraffin-embedded; GGI, Genomic Grade Index; qRT-PCR, quantitative reverse transcription polymerase chain reaction; TAM, tamoxifen.

**MammaPrint**
- **General results**
- **Risk of distant recurrence risk @ 5 years w/ no treatment**

**OncotypeDX**
- **pN0**
  - **Personal results**
  - **Risk of distant recurrence @ 10 years w/ TAM 5 years**
- **pN+**
  - **Risk of distant recurrence @ 5 years w/ TAM 5 years**
• 6,600 pts < 70
  – FEB 2007-AUG 2011
  – 11,291 registered pts
  – 6,673 enrolled (59.1%)
People in their eighties…
OUTCOME DISPARITIES BY AGE AND 21-GENE RECURRENCE SCORE RESULT IN HORMONE RECEPTOR-POSITIVE (HR+) BREAST CANCER

Shak S,1 Miller DP,1 Howlader N,2 Gliner N,1 Howe W,3 Schussler N,3 Cronin K,2 Baehner FL,1,4 Penberthy L,2 Petkov VI2

1. Genomic Health, Inc., Redwood City, CA, USA
2. National Cancer Institute, Rockville, MD, USA
3. IMS, Inc., Calverton, MD, USA
4. University of California, San Francisco, San Francisco, CA, USA

Methods

- SEER demographics, tumor characteristics, reported CT use, and BCSM available through 2013
- Genomic Health provided RS electronically to SEER, per registry operations
- Analysis population: N0, HR+ (by SEER and RT-PCR), HER2-negative (by RT-PCR), diagnosed between January 2004 and December 2012
  - Excluded: N+, prior invasive tumors, or concurrent multiple tumors
- RS groups standard cutpoints (18, 31)
- Actuarial estimates of survival (cause-specific and overall) and BCSM computed through 5 years with 95% CI
- The log-rank test was used to compare the three RS groups
SEER Population - STROBE Diagram

- Diagnosed with primary invasive breast cancer (2004-2012) N=430,519
- HR-positive; non-metastatic n=312,364
- Node-negative n=211,586
- Tested with 21-gene assay n=53,947
- Untested with 21-gene assay\textsuperscript{a} n=157,639
- With Recurrence Score results\textsuperscript{b} n=49,681

\textsuperscript{a} Untested cohort without R5 results includes patients with HER2+ breast cancer because HER2 status was not reported to SEER before 2010.

\textsuperscript{b} Tested cohort with R5 results excludes patients with HER2+ breast cancer, based on 21-gene assay quantitative single-gene HER2 result. Median follow-up for younger (<70 years) and older (\geq70 years) patients were 48 and 40 months, respectively.
Patient Testing and Demographics

<table>
<thead>
<tr>
<th></th>
<th>Age &lt;70 years</th>
<th></th>
<th>Age ≥70 years</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tested (N=43,693)</td>
<td>Not Tested (N=100,519)</td>
<td>Tested (N=5,988)</td>
<td>Not Tested (N=57,120)</td>
</tr>
<tr>
<td>Sex*</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Female</td>
<td>99</td>
<td>99</td>
<td>99</td>
<td>99</td>
</tr>
<tr>
<td>Race</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>White</td>
<td>84</td>
<td>81</td>
<td>87</td>
<td>87</td>
</tr>
<tr>
<td>Black</td>
<td>8</td>
<td>9</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Asian or Pacific Islander</td>
<td>8</td>
<td>10</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Am. Indian/Alaska Native</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Socioeconomic status, quintile</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Lowest SES</td>
<td>11</td>
<td>13</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>Second lowest SES</td>
<td>15</td>
<td>17</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>Middle SES</td>
<td>19</td>
<td>20</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>Second highest SES</td>
<td>23</td>
<td>23</td>
<td>23</td>
<td>22</td>
</tr>
<tr>
<td>Highest SES</td>
<td>32</td>
<td>28</td>
<td>25</td>
<td>25</td>
</tr>
</tbody>
</table>

- Almost 6,000 patients ≥70 years with RS results
- Testing occurred 3.2 times less frequently in patients ≥70 years compared to <70 years
- Testing rates were similar by race and socioeconomic status

* About 0.7% were male.
## Reported Chemotherapy (CT) Use

<table>
<thead>
<tr>
<th></th>
<th>Age &lt;70 years</th>
<th>Age ≥70 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tested (N=43,693)</td>
<td>23%</td>
<td>11%</td>
</tr>
<tr>
<td>Not Tested (N=100,519)</td>
<td>69%</td>
<td>89%</td>
</tr>
<tr>
<td>CT use reported as 'yes'</td>
<td>CT use reported as 'no/unknown'</td>
<td></td>
</tr>
</tbody>
</table>

- CT use was lower in patients ≥70 years, in both RS-tested and untested cohorts.

*Chemotherapy use is known to be under-reported to SEER.*
5-year BCSM by Age and RS Group

- RS predicts BCSM in both age groups (p<0.001)
- Low 5-y BCSM was observed with RS <18 in both age groups
- Higher 5-y BCSM was observed with RS 18-30 and RS ≥31 in older patients

5-year Other-Cause Mortality by Age and RS Group

- As expected, RS group does not predict other-cause mortality (p=NS)
- As expected, higher other-cause mortality was observed in older patients
5-year BCSM (95% CI) by Age in Tested and Untested Patients

<table>
<thead>
<tr>
<th></th>
<th>RS &lt; 18</th>
<th></th>
<th></th>
<th>RS 18-30</th>
<th></th>
<th></th>
<th>RS ≥31</th>
<th></th>
<th></th>
<th>Untested</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>CT Use(^a) (% of N)</td>
<td>5-y BCSM (95% CI)</td>
<td>N</td>
<td>CT Use(^a) (% of N)</td>
<td>5-y BCSM (95% CI)</td>
<td>N</td>
<td>CT Use(^a) (% of N)</td>
<td>5-y BCSM (95% CI)</td>
<td>N</td>
<td>CT Use(^a) (% of N)</td>
<td>5-y BCSM (95% CI)</td>
<td></td>
</tr>
<tr>
<td>&lt;70 y</td>
<td>24050</td>
<td>7%</td>
<td>0.3% (0.2%, 0.5%)</td>
<td>16304</td>
<td>37%</td>
<td>1.2% (0.9%, 1.4%)</td>
<td>3339</td>
<td>73%</td>
<td>4.1% (3.3%, 5.1%)</td>
<td>100519</td>
<td>31%</td>
<td>2.3% (2.2%, 2.4%)</td>
<td></td>
</tr>
<tr>
<td>≥70 y</td>
<td>3424</td>
<td>2%</td>
<td>1.3% (0.8%, 2.1%)</td>
<td>2042</td>
<td>14%</td>
<td>2.6% (1.8%, 3.8%)</td>
<td>522</td>
<td>52%</td>
<td>8.9% (5.8%, 13.4%)</td>
<td>57120</td>
<td>4%</td>
<td>5.5% (5.2%, 5.7%)</td>
<td></td>
</tr>
<tr>
<td>70-74 y</td>
<td>2116</td>
<td>2%</td>
<td>1.1% (0.6%, 2.0%)</td>
<td>1245</td>
<td>17%</td>
<td>2.4% (1.4%, 3.9%)</td>
<td>320</td>
<td>61%</td>
<td>6.2% (3.2%, 11.9%)</td>
<td>17647</td>
<td>8%</td>
<td>2.8% (2.6%, 3.2%)</td>
<td></td>
</tr>
<tr>
<td>75-79 y</td>
<td>968</td>
<td>2%</td>
<td>1.9% (0.9%, 4.0%)</td>
<td>590</td>
<td>11%</td>
<td>2.4% (1.1%, 5.2%)</td>
<td>142</td>
<td>43%</td>
<td>11.6% (5.5%, 23.8%)</td>
<td>16445</td>
<td>4%</td>
<td>4.3% (4.0%, 4.7%)</td>
<td></td>
</tr>
<tr>
<td>≥80 y</td>
<td>340</td>
<td>1%</td>
<td>1.0% (0.2%, 4.5%)</td>
<td>207</td>
<td>6%</td>
<td>4.8% (2.3%, 9.9%)</td>
<td>60</td>
<td>32%</td>
<td>20.5% (9.6%, 40.6%)</td>
<td>23028</td>
<td>2%</td>
<td>8.6% (8.2%, 9.1%)</td>
<td></td>
</tr>
</tbody>
</table>

- Notably, 5-y BCSM is relatively high in untested patients at all ages; this deserves further study.

---

\(^a\) Chemotherapy use reported as ‘yes’ (vs. ‘no/unknown’).
In the absence of significant co-morbidity the MAXIMUM age at which a standard chemotherapy regimen should be advised is...

There is NO absolute age limit. Rather, it depends on the:
1) disease
2) presence of comorbidities
3) life expectancy
4) patient’s preference ... 87.2%
Adjuvant chemotherapy

ASTER 70s

(EUDRACT N° 2011-004744-22, PHRC national 2011, NCT01564056)

ER+ (ongoing study)

Courtesy of Professor Etienne Brain, Immediate Past President of SIOG
Phase III APHINITY Study: Adjuvant Pertuzumab/Trastuzumab/Chemotherapy Increased Invasive Disease–Free Survival in HER2-Positive Breast Cancer

By The ASCO Post
Posted: 3/2/2017 10:55:14 AM
Last Updated: 3/2/2017 10:55:14 AM

APHINITY

N=3800 planned (4800 enrolled)

Central confirmation of HER2 status

Population: Node + or high risk node negative

ACT or TCH

trastuzumab + pertuzumab*
x 1 year

ACT or TCH

tristuzumab + placebo*
x 1 year

*antibody therapy starts with taxane

Andoxanib, Epirubicin, Cyclophosphamide, Taxane (paclitaxel or docetaxel), 5-FU-Fluorouracil, Herstuzumab, Perpertuzumab
Outline

- The undeniable emerging needs
- Current Dilemmas for Elderly BC patients
- Opportunities & Challenges
- Conclusion
Our Future Directions...

Young Patients
“Quantity of life” – to strive to live longer
Family and social obligations

Oncologist’s perspective
Investigations and Treatment
Response and Toxicities
- RECIST
- NCI CTC V 4.0
- Survival (DFS, PFS, OS)
- ”Fast-Moving” world

“Molecular Portrait”
GEP
- Identifying individual patient who can be spared or benefitted from chemo (systemic therapy)

Elderly Patients
Quality of life +++
Independent, and staying at home

Geriatrician’s perspective
Symptoms and Diagnosis
Quality of Survival
- Amount of life with good QoL
- cognition
- functional status
- QoL
- nutrition
“Global Portrait” – aging population

CGA
- Identifying individual elderly patient who will benefit from systemic therapy
Our Future Directions...

**Young Patients**

- “Quantity of life” – to strive to live longer
- Family and social obligations

**Young Patients**

- “Quantity of life” – to strive to live longer
- Family and social obligations

**Oncologist’s perspective**

- Investigations and Treatment
- Response and Toxicities
  - RECIST
  - NCI CTC V 4.0
  - Survival (DFS, PFS, OS)
  - “Fast-Moving” world

**Elderly Patients**

- “Quantity of life” – to strive to live longer
- Family and social obligations
- and staying at home

**Geriatrician’s perspective**

- Diagnosis
- Survival
- Functional status
- “Global Portrait” – aging population

**GEP**

- Identifying individual patient who can be spared or benefitted from chemotherapy

**CGA**

- Identifying individual elderly patient who will benefit from systemic therapy

**Genomic Defect**

- Targeted Therapy

**CGA Defect**

- Targeted Geriatric Intervention
To be practice changing, let us be practice sharing!

From Professor Etienne Brain, Immediate Past President of the SIOG
Acknowledgements

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The Hong Kong Breast Cancer Foundation
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Elderly Breast Cancer – Systemic Therapy

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Hon. Clinical Assistant Professor
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Founding Convenor
Hong Kong Breast Oncology Group
Scientific Committee Meeting
International Society of Geriatric Oncology (SIOG 2017)

20th April, 2017