Long term survival study of de-novo metastatic breast cancers with or without primary tumor resection

Dr. Michael Co
Division of Breast Surgery
Queen Mary Hospital
The University of Hong Kong
Conflicts of interests

- None
- Apart from being a breast surgeon
De novo metastatic breast cancer

• Metastatic breast cancer (MBC) on presentation is diagnosed in less than 10% of all patients

• Treatment is mainly palliative
  – Systemic treatment
  – Symptomatic treatment

• Due to improved systemic treatment
  – Survival of MBC has very much improved

• De novo MBC = Systemic disease

• Surgical resection of primary breast tumor = doubtful survival benefit

• Conflicting results from previous studies
Against:
- Badwe et al. (2015 / RCT)
- King et al. (2016 / Prospective cohort)

For:
- Khan et al. (2002 / Retrospective cohort)
- Babiera et al. (2006 / Retrospective cohort)
- Soran et al. (2016 / RCT)
In the context of de novo MBC

Where are we now?
Where are we heading to?

Aim of this study:

To evaluate the **survival outcome** of MBC treated with or without primary breast tumor resection

To evaluate the **prognosticators** of MBC
Methods

• Institutional review board approval for data access and collection
• Registered retrospective cohort study (# 3485)
  – Prospectively maintained database

• Study period January 2007 – December 2016

• Inclusion criteria
  – All patients with de novo stage IV invasive ductal carcinoma (IDC)
    • With or without resection of the primary breast tumour

• Exclusion criteria
  – Patients with metastatectomy
  – Distant metastasis developed after initial treatment
  – Patients with tumour histology other than IDC were excluded from the analysis.
Treatment of breast cancer

- We adopt standardized treatment
  - National Comprehensive Cancer Network (NCCN) guidelines
  - Multi-disciplinary approach
  - Surgical excision of primary tumor
    - Indications
      - Symptomatic (Bleeding / ulceration / wound problem)
      - Patient wish
    - Patient’s premorbid and performance status
    - All patients received pre-operative anesthetic assessment
Statistical methods

• Survival analysis
  – Kaplan-Meier Method with log rank test

• Univariate analysis
  – Chi-square test, Fisher’s exact test or student T-test where appropriate

• Multivariate analysis with logistic regression

• Statistical significance level of 0.05 was adopted.

• Oligometastasis was defined as number of metastatic site of <=3.
Results

• 1769 IDC patients were identified
  – Of which 172 (9.7%) were de novo stage IV IDC

• Median age of diagnosis
  – 53 years old (Range 24 - 91 years old)

• 91 patients received primary tumour excision (Surgical group)
  – Mastectomy = 86
  – Breast conserving surgery = 5
  – All (N = 91) had clear resection margin (i.e. No tumor at inked margin)

• 81 patients were never treated surgically (Non-surgical group)
Baseline demographics & tumour characteristics
<table>
<thead>
<tr>
<th>Factors</th>
<th>Non-surgical group (n=81)</th>
<th>Surgical group (n=91)</th>
<th>p-value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;= 50</td>
<td>63 (77.8%)</td>
<td>41 (45.1%)</td>
<td></td>
</tr>
<tr>
<td>&lt; 50</td>
<td>18 (22.2%)</td>
<td>50 (54.9%)</td>
<td></td>
</tr>
<tr>
<td>T stage</td>
<td></td>
<td></td>
<td>0.09</td>
</tr>
<tr>
<td>T1</td>
<td>0 (0%)</td>
<td>6 (6.7%)</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>19 (23.5%)</td>
<td>30 (33.3%)</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>8 (9.9%)</td>
<td>7 (7.8%)</td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td>54 (66.7%)</td>
<td>47 (52.2%)</td>
<td></td>
</tr>
<tr>
<td>N stage</td>
<td></td>
<td></td>
<td>0.326</td>
</tr>
<tr>
<td>N0</td>
<td>56 (69.1%)</td>
<td>69 (75.8%)</td>
<td></td>
</tr>
<tr>
<td>N+</td>
<td>25 (30.9%)</td>
<td>22 (24.2%)</td>
<td></td>
</tr>
<tr>
<td>Contralateral axillary metastasis</td>
<td></td>
<td></td>
<td>0.834</td>
</tr>
<tr>
<td>Yes</td>
<td>6 (7.4%)</td>
<td>6 (6.6%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>75 (92.6%)</td>
<td>85 (93.4%)</td>
<td></td>
</tr>
<tr>
<td>No. of site of metastasis</td>
<td></td>
<td></td>
<td>0.42</td>
</tr>
<tr>
<td>1</td>
<td>30 (37.0%)</td>
<td>59 (64.8%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>26 (32.1%)</td>
<td>21 (23.1%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>21 (25.9%)</td>
<td>9 (9.9%)</td>
<td></td>
</tr>
<tr>
<td>4 or above</td>
<td>4 (4.9%)</td>
<td>2 (2.2%)</td>
<td></td>
</tr>
<tr>
<td>Tumour immunohistochemistry</td>
<td></td>
<td></td>
<td>0.628</td>
</tr>
<tr>
<td>ER + HER2 +</td>
<td>20 (26.0%)</td>
<td>27 (30.3%)</td>
<td></td>
</tr>
<tr>
<td>ER + HER2 -</td>
<td>37 (48.1%)</td>
<td>41 (46.1%)</td>
<td></td>
</tr>
<tr>
<td>ER - HER2 -</td>
<td>13 (16.9%)</td>
<td>17 (19.1%)</td>
<td></td>
</tr>
<tr>
<td>TNBC</td>
<td>7 (9.1%)</td>
<td>4 (4.5%)</td>
<td></td>
</tr>
<tr>
<td>Pre-morbid (ASA score)</td>
<td></td>
<td></td>
<td>0.355</td>
</tr>
<tr>
<td>1 &amp; 2</td>
<td>44 (54.3%)</td>
<td>43 (47.3%)</td>
<td></td>
</tr>
<tr>
<td>3 or above</td>
<td>37 (45.7%)</td>
<td>48 (52.7%)</td>
<td></td>
</tr>
<tr>
<td>Hormonal therapy</td>
<td></td>
<td></td>
<td>0.267</td>
</tr>
<tr>
<td>Yes</td>
<td>56 (69.1%)</td>
<td>69 (76.7%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>25 (30.9%)</td>
<td>21 (23.3%)</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy / Targeted therapy</td>
<td></td>
<td></td>
<td>0.101</td>
</tr>
<tr>
<td>Yes</td>
<td>37 (45.7%)</td>
<td>54 (60%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Survival outcome of MBC

- 2-year overall survival (OS) of MBC = 79.4%
- The 5-year OS of MBC = 38.9%
- The median survival time = 48 months
• 2-year OS
  – Surgical group = 84.5%
  – Non-surgical group = 73.7%

• The 5-year OS
  – Surgical group = 43.9%
  – Non-surgical group = 33.9%
  – Log-rank test \( (p = 0.026) \)

• Median survival time
  – Surgical group = 55 months
  – Non-surgical group = 40 months
Oligometastasis and its survival

Median survival duration (Months)

- 1 metastatic site (N = 89): 69
- 2 metastatic sites (N = 47): 47
- 3 metastatic sites (N = 30): 38
- 4 metastatic sites (N = 5): 48
- 5 metastatic sites (N = 1): 61

Log-rank test, $p = 0.072$
<table>
<thead>
<tr>
<th>Variables</th>
<th>Hazard Ratio (HR)</th>
<th>p-value</th>
<th>95%CI for HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;= 50 at diagnosis</td>
<td>1.034</td>
<td>0.005</td>
<td>(1.010, 1.058)</td>
</tr>
<tr>
<td>ER Positivity</td>
<td>0.420</td>
<td>0.001</td>
<td>(0.256, 0.688)</td>
</tr>
<tr>
<td>HER2 Positivity</td>
<td>0.626</td>
<td>0.052</td>
<td>(0.391, 1.004)</td>
</tr>
<tr>
<td>Visceral (Lung or liver) metastasis</td>
<td>1.672</td>
<td>0.038</td>
<td>(1.028, 2.719)</td>
</tr>
<tr>
<td>Brain metastasis</td>
<td>2.808</td>
<td>0.058</td>
<td>(0.964, 8.183)</td>
</tr>
<tr>
<td>Oligometastasis</td>
<td>3.27</td>
<td>0.677</td>
<td>(1.272, 8.400)</td>
</tr>
<tr>
<td>Locally advanced primary (T3 or above)</td>
<td>1.126</td>
<td>0.753</td>
<td>(0.537, 2.361)</td>
</tr>
</tbody>
</table>
Limitations of this study

• Retrospective study
  – Selection bias / confounders

• However
  – The analysis was based on a sizable cohort
  – Prospectively maintained database
  – Comparable baseline demographic characteristics
Conclusions

While 5-year OS in de novo metastatic breast cancer remains poor

Surgical resection of the primary tumour may confer survival benefit in carefully selected patients
• Where are we now?
  – Era of much improved systemic treatment

• Where are we heading to?
  – Expecting an expanding role of surgical treatment in MBC
THANK YOU

Dr. Ava Kwong

& all team members