Prognostic value of lung cancer mutation status in patients undergoing surgical resection of brain metastases

Yuhao (Danny) Huang, Kevin K.H. Chow, Jacqueline V. Aredo, Summer Han, Melanie H. Gephart

Department of Neurosurgery
AANS 2018
Disclosure

We have no conflict of interest to disclose
Background

- Brain metastasis is a common complication for patients with non-small cell lung cancer (NSCLC)

- Surgical resection of solitary brain lesion in addition to radiotherapy has been shown to improve survival and quality of life

- However, few prognostic markers have been identified for NSCLC patients undergoing neurosurgical resection of brain lesions

Molecular stratification and tyrosine kinase inhibitors

Chemo/Immunotherapy

\[
\text{Cl}_2\text{Pt}\text{NH}_3
\]

\[
\text{Cl}\text{NH}_3
\]

KRAS mutation

WT

Tumor Sample

EGFR mutation

Erlotinib

Does mutation status impact the survival of patients undergoing neurosurgical resection?

Crizotinib

EML-ALK fusion
Database: STRIDE database at Stanford University
- January 1996 to May 2016

Inclusion Criteria
- Diagnosis of primary lung cancer
- Craniotomy performed for resection of brain metastasis

Primary Outcome
- Overall survival (OS) from date of craniotomy to date of last follow-up
STRIDE Database
Jan 1996 - May 2016
N=250 patients

Mutation status available
N=84 patients

No somatic mutation panel or FISH studies
N=166 patients

Lost to follow-up
N=4 patients

WT
N=35 patients (43.8%)

EGFR
N=29 patients (36.3%)

KRAS
N=11 patients (13.8%)

ALK
N=5 patients (6.3%)
# Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All patients (N=80)</th>
<th>P-value (across mutation status)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis, Range</td>
<td>61 (35-90)</td>
<td>0.19</td>
</tr>
<tr>
<td>Male sex, No. (%)</td>
<td>36 (45.0)</td>
<td>0.13</td>
</tr>
<tr>
<td>White race, No. (%)</td>
<td>49 (61.2)</td>
<td>0.19</td>
</tr>
<tr>
<td>Smoking, No. (%)</td>
<td>52 (65.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Histology (adenocarcinoma), No. (%)</td>
<td>74 (92.5)</td>
<td>0.69</td>
</tr>
<tr>
<td>Onset (synchronous), No. (%)</td>
<td>47 (58.8)</td>
<td>0.73</td>
</tr>
<tr>
<td>Time to craniotomy (&gt;1mth), No. (%)</td>
<td>20 (25.0)</td>
<td>0.11</td>
</tr>
<tr>
<td>Targeted Therapy, No. (%)</td>
<td>36 (45.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Solitary Lesion, No. (%)</td>
<td>26 (32.5)</td>
<td>0.60</td>
</tr>
<tr>
<td>Prev. Lung Resection, No. (%)</td>
<td>17 (21.2)</td>
<td>0.68</td>
</tr>
<tr>
<td>Controlled Primary, No. (%)</td>
<td>22 (27.5)</td>
<td>0.91</td>
</tr>
<tr>
<td>RPA Class I, No. (%)</td>
<td>8 (10.0)</td>
<td>0.13</td>
</tr>
<tr>
<td>GPA Score 0-1.0, No. (%)</td>
<td>14 (17.5)</td>
<td>0.08</td>
</tr>
<tr>
<td>History of cranial XRT, No. (%)</td>
<td>18 (22.5)</td>
<td>0.25</td>
</tr>
<tr>
<td>Post-operative XRT, No. (%)</td>
<td>66 (82.5)</td>
<td>0.61</td>
</tr>
<tr>
<td>Patient Alive, No. (%)</td>
<td>32 (40.0)</td>
<td>0.37</td>
</tr>
</tbody>
</table>
EGFR+ mutation is associated with increased survival post-neurosurgery

<table>
<thead>
<tr>
<th>Mutation</th>
<th>Median Survival</th>
<th>Univariate HR (95% CI)</th>
<th>Multivariate HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>WT</td>
<td>21</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>EGFR</td>
<td>58</td>
<td>0.47 (.24-0.93)</td>
<td>0.25 (.0.07-.87)</td>
</tr>
<tr>
<td>KRAS</td>
<td>34</td>
<td>0.65 (.25-1.69)</td>
<td>0.61 (.21-1.72)</td>
</tr>
<tr>
<td>ALK</td>
<td>40</td>
<td>1.23 (.42-3.57)</td>
<td>0.82 (.17-3.97)</td>
</tr>
</tbody>
</table>
Patients with a history of WBRT have poorer survival after neurosurgery

<table>
<thead>
<tr>
<th>History of XRT</th>
<th>Median Survival</th>
<th>Univariate HR (95% CI)</th>
<th>Multivariate HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>30</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
</tr>
<tr>
<td>SRS</td>
<td>31</td>
<td>1.48 (0.57-3.81)</td>
<td>1.27 (.21-7.85)</td>
</tr>
<tr>
<td>WBRT</td>
<td>10</td>
<td>7.00 (2.51-19.56)</td>
<td>5.02 (1.24-20.32)</td>
</tr>
<tr>
<td>SRS and WBRT</td>
<td>5</td>
<td>7.68 (2.58-22.89)</td>
<td>9.99 (2.03-49.32)</td>
</tr>
</tbody>
</table>
EGFR mutation is an independent predictor of improved survival after craniotomy for resection of NSCLC brain metastasis

Exposure to whole-brain radiation therapy prior to neurosurgery was associated with poor survival. The risk of mortality was even higher in patients who received both whole-brain radiation therapy and stereotactic radiosurgery.