Real-world data analysis of genomic profiling-matched targeted therapy outcomes in patients with advanced fusion-positive NSCLC

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INTRODUCTION

• Clinical oncology societies recommend the use of Comprehensive Genomic Profiling (CGP) to identify patients eligible for matched targeted therapy, yet full utilization of the potential benefits of CGP has not occurred in routine clinical practice.
• Here we assess the adherence to ESMO matched targeted therapy recommendations and associated outcomes for CGP-based ALK, RET, ROS1, and NTRK fusions detected in a large real-world, observational dataset of advanced NSCLC patients.

METHODS

Data Sources:
• De-identified stage IV or metastatic NSCLC records from the Tempus database were retrospectively analyzed.
• The database encompasses molecular and clinical data from hundreds of clinics across the United States sequenced with the Tempus XT assay (DNA and whole exome capture RNA) from 2018 - 2022.

Definitions and Statistical analysis:
• Real-world overall survival (rwOS) was defined as the interval from start of medication prescribed after sequencing to date of death, censored on the last known physician encounter.
• A cox proportional hazards model was fit to evaluate the relationship between matched targeted therapy compliance and rwOS in fusion-positive patients.

RESULTS

Table 1. Cohort Demographics and Characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Guideline Recommended</th>
<th>Non-guideline Treatment</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Sequencing (Median [IQR])</td>
<td>65 (54, 69)</td>
<td>60 (58, 76)</td>
<td>0.04</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>31 (50.5%)</td>
<td>22 (41.5%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Female</td>
<td>24 (41.9%)</td>
<td>29 (53.9%)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>16 (10.9%)</td>
<td>14 (18.4%)</td>
<td>0.50</td>
</tr>
<tr>
<td>Black</td>
<td>24 (15.1%)</td>
<td>30 (49.1%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>16 (10.9%)</td>
<td>12 (20.0%)</td>
<td>0.17</td>
</tr>
<tr>
<td>White</td>
<td>12 (7.5%)</td>
<td>4 (6.7%)</td>
<td></td>
</tr>
<tr>
<td>Smoking Status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-smoker</td>
<td>33 (54.0%)</td>
<td>30 (56.6%)</td>
<td>0.31</td>
</tr>
<tr>
<td>Smoker</td>
<td>24 (41.9%)</td>
<td>13 (24.5%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>5 (8.3%)</td>
<td>1 (1.9%)</td>
<td></td>
</tr>
<tr>
<td>Cellular Pathology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>43 (69.1%)</td>
<td>33 (58.3%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Adenosquamous</td>
<td>5 (8.1%)</td>
<td>5 (8.1%)</td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>15 (24.5%)</td>
<td>12 (20.0%)</td>
<td></td>
</tr>
<tr>
<td>Neoadjuvant chemotherapy</td>
<td>1 (1.9%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>30 (48.3%)</td>
<td>21 (41.7%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Chemoradiation</td>
<td>12 (20.0%)</td>
<td>13 (24.5%)</td>
<td></td>
</tr>
<tr>
<td>Sequencing to Medication Start (Median [IQR])</td>
<td>285.1 (150.0, 360.3)</td>
<td>283.5 (150.0, 360.3)</td>
<td>0.96</td>
</tr>
<tr>
<td>Sequencing to Last Known Date (Median [IQR])</td>
<td>391 (225.0, 573.0)</td>
<td>376 (225.0, 550.0)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Figure 2. Distribution of Guideline Recommended Medications.

A: Guideline Recommended
- Alectinib
- Bcr-Abl1
- Crizotinib
- Cetuximab
- Cisplatin
- Gefitinib
- Erlotinib
- Lapatinib
- Sorafenib
- Tarceva

B: Non-guideline Treatment
- Docetaxel
- Bevacizumab
- Pembrolizumab
duvlumab
- Nilotinib
- Carboplatin

Figure 3. Proportion of Fusion Patients on CGP-matched Guideline Recommended Therapy.

The overall compliance rate of targeted therapy was 82% (N=53).

Figure 4. Survival from Start of Medication.

A: All Fusions
- Non-guideline treatment
  - At Risk: 52
  - Censored: 23
  - Events: 1
- Guideline recommended
  - At Risk: 31
  - Censored: 11
  - Events: 1

B: ALK fusions
- Non-guideline treatment
  - At Risk: 43
  - Censored: 11
  - Events: 9
- Guideline recommended
  - At Risk: 22
  - Censored: 12
  - Events: 2

[1] Wiscon test
[2] Cochrane test

REFERENCES