Prevalence of EGFR T790M mutation in NSCLC patients after atafinib failure, and subsequent response to osimertinib

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**Background**

- Targeted treatment with first- or second-generation EGFR TKIs has become the standard of care for patients with advanced NSCLC harboring EGFR exon 19 deletion (Del19+) or EGFR L858R mutation
- Prevalence of EGFR T790M mutation was reported around 40–60% in patients who progressed after treatment with first- or second-generation TKIs
- EGFR T790M mutation can be acquired during treatment with first-generation TKIs

**Methods**

- This single-center, real-world analysis included all patients who progressed between April 2015 and April 2017
- The data were analyzed in a descriptive retrospective approach

**Objective**

To identify the prevalence of EGFR T790M mutation in patients who progressed after treatment with afatinib

**Baseline characteristics**

- Median age was 65 years (range: 40–82), and 75% of patients were smokers
- Majority of patients (76%) received first-line treatment with afatinib

**Baseline characteristics for the overall cohort**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number (N=48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65 (40–82)</td>
</tr>
<tr>
<td>Gender</td>
<td>Male 25 (52%)</td>
</tr>
<tr>
<td>Race</td>
<td>Caucasian 35 (72%)</td>
</tr>
<tr>
<td>Smoking status</td>
<td>Current smokers 15 (31%)</td>
</tr>
<tr>
<td>Smoking status</td>
<td>Ex-smokers 10 (21%)</td>
</tr>
<tr>
<td>Smoking status</td>
<td>Never smokers 23 (48%)</td>
</tr>
<tr>
<td>Never smokers (N=140)</td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td>Current smokers 49 (35%)</td>
</tr>
<tr>
<td>Ex-smokers</td>
<td>32 (23%)</td>
</tr>
<tr>
<td>Never smokers</td>
<td>59 (42%)</td>
</tr>
</tbody>
</table>

**Results**

- EGFR T790M mutation was present in 81% of patients who progressed after treatment with afatinib
- ORRs were higher than in previous studies, as this analysis only included patients who had achieved ≥3 months disease control with afatinib

**Efficacy**

- ORR with osimertinib was 81% among the 27 patients who had acquired T790M mutation after afatinib

**Conclusions**

- Osimertinib after first-line afatinib may be an effective treatment option for patients with EGFR T790M mutation
- Further data on resistance mechanisms to afatinib are needed

**References**

7. Afatinib improved OS versus chemotherapy in Del19+ patients in Phase III studies
8. In the Phase I/II AURA study, 68% of patients with acquired resistance had the T790M mutation
9. Most patients in this study had received erlotinib and gefitinib as first- and second-generation TKIs
10. In a Phase III study, osimertinib significantly improved PFS and ORR versus chemotherapy in patients with ≥3 months disease control with afatinib
11. EGFR T790M mutation can be acquired during treatment with first-generation TKIs
12. Median time on sequential treatment with afatinib and osimertinib was 25.0 months (95% CI: 20–33 months)

Prevalence of acquired T790M mutation

- In this single-center, real-world analysis, the prevalence of EGFR T790M mutation was present in 81% of patients who progressed after initially achieving ≥3 months disease control with afatinib
- This is consistent with prevalence rates of 48–66% in previous analyses of patients with acquired resistance to afatinib, and 46–58% among patients who progressed on first-generation TKIs

Efficacy of osimertinib

- ORRs were higher than in previous studies, as this analysis only included patients who had achieved ≥3 months disease control with afatinib
- Rates of response to afatinib were high (ORR 90%), although duration of response (CR, PR, or SD) did not appear to correlate with baseline characteristics
- For patients receiving afatinib in the second or third line, it is not known when the EGFR T790M mutation emerged, as testing took place after failure on atafinib therapy
- Response to osimertinib and atafinib
- Rates of response to afatinib were high (ORR 90%), although this analysis only included patients who had achieved ≥3 months disease control with afatinib
- Osimertinib was effective in 56% of patients with EGFR T790M mutation after afatinib

**Key findings and conclusions**

- Osimertinib after first-line afatinib may be an effective treatment option for patients with EGFR T790M mutation
- Further data on resistance mechanisms to afatinib are needed

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**Data were previously presented: Hochmair, et al. OGP 2017, poster #P55. *Corresponding author email address: Maximilian.Hochmair@wienkav.at**