Background:
- Brigatinib and alectinib are both next-generation ALK inhibitor (ALKi) and first-line standard of care options in advanced ALK-rearranged NSCLC patients (ALK+ aNSCLC), with efficacy established by phase 3 trials (1,2).
- In the management of ALKi therapeutic sequence, many questions remain about the efficacy of second-generation ALKi in the event of discontinuation due to progression or toxicity of a previous second-generation ALKi.
- The objective of Brigale was to describe in a real-world setting the efficacy of alectinib post-brigatinib in patients with advanced NSCLC harboring ALK rearrangement, pretreated with at least one ALKi inhibitor.

Patients and methods:
- BrigALK2 is an ancillary study of BrigALK2 that focused on alectinib efficacy after brigatinib treatment, according to post-brigatinib treatment line in BrigALK2.
- BrigALK2, a national non-interventional multicenter study, evaluated BrigAlec efficacy in 183 ALK+ aNSCLC patients, pretreated with at least one ALKi inhibitor (ALKi), during brigatinib French early access program, from 1st August 2016 to 21st January 2019 (3).
- Patient characteristics, alectinib duration of treatment (DOT) and progression-free survival according to investigators (invPFS), response rate, disease control rate and reasons for discontinuation were collected from the medical files.

Results:
- 92 (50.3%) patients received ≥1 agent(s) post-brigatinib.
- 30 (16.4%) received alectinib regardless of treatment line post-brigatinib.
- 19 were treated with alectinib immediately after brigatinib (brigatinib-alectinib sequence) and 11 following at least one line of treatment (chemotherapy (chemo) or another ALKi: brigatinib-X alectinib sequence), table 1.
- At data cut-off (07/07/2022), median follow-up was 25.5 (95% CI: 10.6-30.5) months.
- Data about mutations of resistance post-brigatinib exposure were very scarce and not usable.

For patients treated according to brigatinib-alectinib sequence (table 1):
- mDOT, miniPFS and mOS were 7.1 (95%CI: 2.1-18.2), 4.8 (95%CI 2.0-12.5) and 27 (95%CI: 12.5-59) months, respectively, from the start of alectinib.
- Response and disease control rates were 25% and 60% respectively.
- Among this subgroup, reasons for discontinuation were toxicity for 5 patients: with a mDOT and miniPFS of 18.2 (95%CI 3.4-21.6) and 12.5 (95%CI: 3.3-17.9) months. 14 patients discontinue brigatinib due to progressive disease, with a mDOT and miniPFS of 5.7 (95%CI: 0.9-10.9) and 3.4 (95%CI 0.9-9.2) months.

Patients treated with alectinib post-brigatinib: n=30

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Patients treated with alectinib post-brigatinib: n=30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>Brigatinib-alectinib sequence</td>
</tr>
<tr>
<td>n=19</td>
<td>7,1 (2,1-18,2)</td>
</tr>
<tr>
<td>n=11</td>
<td>mDOT, months</td>
</tr>
<tr>
<td>mFSS, months</td>
<td>4,8 (2-12,5)</td>
</tr>
<tr>
<td>mOS, months</td>
<td>27,0 (12,5-NR)</td>
</tr>
<tr>
<td>RR, %</td>
<td>25</td>
</tr>
<tr>
<td>DCR, %</td>
<td>60</td>
</tr>
</tbody>
</table>

Conclusion: According to our retrospective real-life study, alectinib after brigatinib treatment remains an option in metastatic ALK+ NSCLC, especially if brigatinib is discontinued due to toxicity.

References:

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