INDIRECT COMPARISON OF BRIGATINIB VERSUS ALECTINIB IN THE ALK-POSITIVE NON-SMALL CELL LUNG CANCER

New abstract number: 1ISG-021
ATC code: L01 - Cytostatics
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BACKGROUND AND IMPORTANCE
ALK gene mutation occurs in 3-5% of patients with non-small cell lung cancer (NSCLC). Brigatinib and Alectinib are potent ALK tyrosine kinase inhibitors, indicated in NSCLC.

AIM AND OBJECTIVES
To perform an adjusted indirect treatment comparison (ITC) of the efficacy of Brigatinib and Alectinib in patients with NSCLC using a common comparator, and to establish whether both ALK inhibitors can be declared equivalent therapeutic alternatives (ETA).

MATERIALS AND METHODS
A search was carried out to detect clinical trials (CT) with Brigatinib or Alectinib with similar population, endpoints and follow-up period.

If multiple studies were found for the same drug. The results were combined in a meta-analysis using the Metasurv-calculator.

ITC
Bucher’s method
To establish the positioning the ETA guidelines was applied.

Delta value = maximum acceptable difference as a clinical criterion of no-inferiority.

0.64 (and its inverse: 1.57) for progression-free survival (PFS).

RESULTS
CT = 4
• Brigatinib (n=1)
• Alectinib (n=3).

1. Phase III
2. Randomised
3. Open-label
4. Crizotinib-controlled
5. Alk-positive NSCLC

The endpoint was PFS (for asian and non-Asian patients).

* Alectinib trials were pooled for asian patients for the PFS.

<table>
<thead>
<tr>
<th>Reference</th>
<th>CT</th>
<th>PFS: HR (95% CI)</th>
<th>ITC: HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alectinib (Asian)</td>
<td>CT1</td>
<td>0.46 (0.28-0.75)</td>
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<tr>
<td></td>
<td>CT2</td>
<td>0.37 (0.22-0.61)</td>
<td>0.95 (0.44-2.08)</td>
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<td></td>
<td>CT3</td>
<td>0.34 (0.21-0.54)</td>
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</tr>
<tr>
<td></td>
<td>Pooled</td>
<td>0.29 (0.29-0.51)</td>
<td></td>
</tr>
<tr>
<td>Brigatinib (Asian)</td>
<td>CT4</td>
<td>0.41 (0.20-0.86)</td>
<td></td>
</tr>
<tr>
<td>Alectinib (non-Asian)</td>
<td>CT1</td>
<td>0.49 (0.32-0.75)</td>
<td>0.91 (0.47-1.75)</td>
</tr>
<tr>
<td>Brigatinib (non-Asian)</td>
<td>CT4</td>
<td>0.40 (0.33-0.90)</td>
<td></td>
</tr>
</tbody>
</table>

The probability of the result being above or below the delta margin

Asian patients: 10.28% and 15.7%
No-asian patients: 5.92% and 14.43%

CONCLUSION AND RELEVANCE
ITC showed no statistically differences in PFS between Brigatinib and Alectinib for asian and non-Asian patients. The extent of 95% CI showed some uncertainty. According to ETA guidelines, since the percentage outside the delta margin is small, both drugs could be considered as ETA in most patients with ALK-positive NSCLC.