EPIDEMOLOGICAL, CLINICAL AND HUMANISTIC BURDEN AMONG ALK+ NON-SMALL CELL LUNG CARCINOMA (ALK+ NSCLC) PATIENTS TREATED WITH FIRST-LINE ALK INHIBITORS: RESULTS OF A SYSTEMATIC LITERATURE REVIEW (SLR)

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Quality of life

- Among the 25 studies that reported QoL data, EORTC QLQ-C30 or QLQ-LC13 were the main QoL instruments (Figure 2).
- Eight studies (5 economic studies and 3 QoL studies) reported utility values in the stable disease phase. Anaplastic lymphoma kinase-positive metastatic non-small cell lung cancer patients treated with first-line ALK inhibitors, QoL diminished with disease progression, utility values ranged from 0.6 to 0.8 in stable patients, and 0.6 to 0.9 in those with first-line ALK inhibitors versus from 0.5 to 0.5 in those with progression (Table 2).

Table 2. Utility Values in Stable Disease/On Treatment and Progressive Disease

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Health-Related Quality of Life (HRQoL) and Utility Results (with Mean and Standard Deviation)</th>
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<td>Reference</td>
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</tr>
<tr>
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2 Conclusions

- This SLR suggests that currently real-world used first-line ALK inhibitors showed poor survival rates and short PFS among ALK+ NSCLC patients.
- EORTC QLQ-C30 or QLQ-LC13 were the main QoL instruments to measure QoL and HRQoL in ALK+ NSCLC patients.
- Disease progression was associated with reduced patient QoL.
- These results indicate a need for more effective first-line treatments for ALK+ NSCLC.

Limitations

- The majority of studies included in this SLR investigated crizotinib as a first-line ALK-Inhibitor. This is due to the fact that alectinib and ceritinib were only recently approved as first-line ALK inhibitors and consequently there is a lack of economic evaluations, humanistic and health-related QoL evidence, and consequently there is a lack of evidence from RWE studies, consequently the data were heterogeneous, with wide variability in study methods, outcome measurements, and patient characteristics. Weighted averages were calculated considering this methodological issue. However, they were not adjusted for other patient characteristics, which may have introduced bias.
- In order to capture clinical outcomes with first-line ALK inhibitors, this study included clinical outcomes from clinical trials and RWE studies, less dimensional and less statistically robust. Patient numbers and consequently limited patient information for several studies made it difficult to overcome the differences in patient numbers, weighted averages were calculated.

Table 1. Weighted Averages of clinical outcomes with first-line ALK inhibitors

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Materials & methods

- A systematic literature review (SLR) following PRISMA guidelines with scope defined in terms of PICOS criteria (Population, Intervention, Comparator, Outcomes, Study Design and Study setting).
- PICOS: Population: The population included adult patients who developed ALK+ NSCLC, regardless of time of ALK rearrangement confirmation, including patients with prior ALK inhibitor use. Studies that were not performed in humans were excluded.
- Interventions: All studies investigating first-line use of ALK inhibitors approved in this setting (crizotinib, alectinib, ceritinib) were included. Additionally, studies in which no interventions were described, for instance epidemiological studies, were included.
- Outcomes: Studies with real-world effectiveness (overall survival, progression-free survival, and objective response rate), epidemiology data, quality of life and utilities were included. Descriptive studies without any outcomes were also included if deemed relevant.
- Study design: This SLR considered well-conducted prospective and retrospective studies, such as observational studies, registries, retrospective analyses of Medical Oncology (ESMO), and non-interventional studies as real-world evidence. Additionally, studies reporting health-related quality of life (HRQoL) and utility data were included. Randomized controlled trials were identified to review potential MRQoL data. Economic studies were reviewed to capture usable utilities and HRQoL of patients with ALK+ NSCLC.
- The following literature databases were searched through the OVID platform from January 2008 to September 2018:
  - Ovid Medline (1950–) (OvidSP)
  - Ovid Embase (1980–) (OvidSP)
  - Ovid Cochrane Database (Collaboration databases)

- To ensure latest studies were also included, abstracts from relevant conferences from 2016 to 2018 were included in the search:
  - American Society of Clinical Oncology (ASCO)
  - European Society for Medical Oncology (ESMO)
  - International Association for the Study of Lung Cancer (IASLC)
  - European Lung Cancer Congress (ELCC)
  - International Society for Pharmacoeconomics and Outcomes Research (ISPOR)
  - Academy of Managed Care Pharmacy (AMCP)
  - International Association for the Study of Lung Cancer World Conference on Lung Cancer (WCLC)
  - American Association for Cancer Research (AACR)
  - Clinicaltrials.gov and public Health Technology Assessment websites (NICE, SMC, CADTH and PBAC) were also searched for additional information.
- The bibliographies of relevant meta-analyses and SRs were searched to retrieve useful literature.
- Publications identified through the systematic review were evaluated to assess whether they should be included for data extraction.
- Data from included studies were extracted into an Excel-based data extraction template.
- Weighted averages of patient characteristics and clinical outcomes were determined among studies investigating approval first-line ALK inhibitors (crizotinib, alectinib, and ceritinib) in ALK+ NSCLC.

Results

- In total, there were 285 records reporting 278 original studies. Of these, 215 reports were from U.S. (78.5%) and 10 reports were from other countries. A study of crizotinib versus ceritinib in first-line (ALTA-11 study) is currently ongoing (NCT02375501) and the result of the 1st interim analysis has been published (Camidge, et al., 2018).
- Although there has been development and approval of new generations of ALK inhibitors in the past few years, the literature is sparse on unmet need and economic and humanistic burden among ALK+ NSCLC patients receiving first-line ALK inhibitors.

Objectives

- The objective of this study was to assess current evidence on epidemiological, clinical and humanistic burden among ALK+ NSCLC patients receiving approved first-line ALK inhibitors.

Background

- Worldwide, lung cancer has been the most common cancer for several decades and 11.6% of new cancer cases were lung cancer in 2018 (GLOBOCAN, 2019).
- Among lung cancer subtypes, approximately 5% of non-small cell lung cancer (NSCLC) cases are anaplastic lymphoma kinase-positive (ALK+) and can benefit from targeted ALK inhibitor treatment (NCCN, 2019).
- The American Society of Clinical Oncology (ASCO) recommends crizotinib and the European Society for Medical Oncology (ESMO) recommends crizotinib, alectinib, ceritinib, and brigatinib as first-line therapy for ALK+ NSCLC (Hanna, et al., 2017; Planchard, et al., 2018). The National Comprehensive Cancer Network (NCCN) also recommends alectinib, ceritinib, and crizotinib as first-line therapy. Among them, alectinib is recommended as a preferred first-line therapy for ALK- NSCLC (NCCN, 2019).
- Crizotinib, alectinib and ceritinib were approved for the first-line treatment of ALK+NSCLC in the U.S. and other countries.
- A study of crizotinib versus ceritinib in first-line (ALTA-11 study) is currently ongoing (NCT02375501) and the result of the 1st interim analysis has been published (Camidge, et al., 2018).

Study sponsored by Takeda Pharmaceutical Company Limited

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