The objectives were twofold:
- To identify products indicated for treatment of non-small-cell lung carcinoma (NSCLC) approved with a PRO labeling claim in Europe and the USA; and
- To list the differences found in Europe vs. the USA in terms of products and labeling.

METHODS

- The PROLabels database was searched for NSCLC products.
- The analysis was performed on medicinal product labels approved by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) as well as on FDA medical reviews and EMA scientific discussions.

RESULTS

- A total of 15 products (generics excluded) were identified (see Table 1):
  - six at the EMA, and
  - nine at the FDA.
- The six products approved by the EMA were also approved by the FDA (i.e., bevacizumab, docetaxel, erlotinib, gefitinib, paclitaxel, and pemetrexed disodium).
- Four products with a PRO claim were identified in Europe (i.e., docetaxel, erlotinib, gefitinib and paclitaxel), and two in the USA (i.e., paclitaxel and gemcitabine).
- Most of the PROs identified in the claims were "quality of life" and "symptoms.
- For four products (i.e., docetaxel, erlotinib, gefitinib and paclitaxel), the EMA and FDA showed disagreement in terms of their PRO labeling. The EMA gave a PRO claim ("quality of life" and "symptoms") to three products, but not the FDA; For paclitaxel, the FDA did not include a "quality of life" claim in the label. Except for gefitinib, the reviews of both agencies were conducted on the same clinical studies. The analysis of the medical reviews and scientific discussions showed that the FDA did not include the PROs in the label because of concerns about the quality of the study design, of the analyses, or the questionnaires’ content validity.

CONCLUSION

- Our review showed that the patients’ perspective in the treatment of non-small-cell lung carcinoma is important for the EMA and FDA. However, differences exist in the evaluation of PRO data for inclusion in the label.
- Our analysis suggests a higher receptivity of the EMA to quality of life as a global concept.

### Table 1. Products approved for the treatment of NSCLC (EMA and FDA)

<table>
<thead>
<tr>
<th>Reference Number(s)</th>
<th>Regulatory Agency</th>
<th>INN</th>
<th>Brand Name</th>
<th>MAH</th>
<th>Date of Approval</th>
<th>PRO Claim</th>
</tr>
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<tbody>
<tr>
<td>EMEA/HC/200582</td>
<td>EMA</td>
<td>bevacizumab</td>
<td>Avastin</td>
<td>Roche Registration</td>
<td>9/12/2005</td>
<td>No</td>
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<td>BLA 125685</td>
<td>FDA</td>
<td></td>
<td>Genentech</td>
<td></td>
<td>26/02/2004</td>
<td>No</td>
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<tr>
<td>EMEA/HC/200584</td>
<td>EMA</td>
<td>pemetrexed disodium</td>
<td>Alimta</td>
<td>Eli Lilly</td>
<td>20/08/2004</td>
<td>No</td>
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<tr>
<td>NDA 021462</td>
<td>FDA</td>
<td></td>
<td></td>
<td>04/02/2004</td>
<td>No</td>
<td></td>
</tr>
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<td>EMEA/HC/200216</td>
<td>EMA</td>
<td>paclitaxel</td>
<td>Paclasure</td>
<td>Mead Johnson</td>
<td>19/07/1998</td>
<td>Yes</td>
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<tr>
<td>NDA 02282</td>
<td>FDA</td>
<td></td>
<td>Taxol</td>
<td></td>
<td>29/12/1992</td>
<td>Yes</td>
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<tr>
<td>EMEA/HC/200073</td>
<td>EMA</td>
<td>docetaxel</td>
<td>Taxotere</td>
<td>Aventis Pharma</td>
<td>27/11/1995</td>
<td>Yes</td>
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<tr>
<td>NDA 02449</td>
<td>FDA</td>
<td></td>
<td>Sandi Aventis</td>
<td></td>
<td>14/05/1996</td>
<td>No</td>
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<td>EMEA/HC/200841</td>
<td>EMA</td>
<td>erlotinib</td>
<td>Tarceva</td>
<td>Roche Registration</td>
<td>19/06/2005</td>
<td>Yes</td>
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<tr>
<td>NDA 021754</td>
<td>FDA</td>
<td></td>
<td>Osi Pharma</td>
<td></td>
<td>18/11/2004</td>
<td>No</td>
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<tr>
<td>EMEA/HC/200106</td>
<td>EMA</td>
<td>gefitinib</td>
<td>Iressa</td>
<td>Astra Zeneca</td>
<td>24/06/2009</td>
<td>Yes</td>
</tr>
<tr>
<td>NDA 021399</td>
<td>FDA</td>
<td></td>
<td></td>
<td>05/05/2003</td>
<td>No</td>
<td></td>
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<tr>
<td>NDA 02570</td>
<td>FDA</td>
<td>crizotinib</td>
<td>Xalkori</td>
<td>Pfizer</td>
<td>26/06/2011</td>
<td>No</td>
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<tr>
<td>NDA 02509</td>
<td>FDA</td>
<td>gemcitabine monohydrate</td>
<td>Gemzar</td>
<td>Eli Lilly</td>
<td>15/05/1998</td>
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<td>NDA 020451</td>
<td>FDA</td>
<td>pofimer sodium</td>
<td>Photofin</td>
<td>Axcan Scandinpharm</td>
<td>27/10/1995</td>
<td>No</td>
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</table>

Quality of life outcomes differed according to EGFR mutation status. In EGFR mutation-positive patients, significantly more RRESSA-treated patients experienced an improvement in quality of life and lung cancer symptoms vs. carboplatin/paclitaxel. In the PASS trial, RRESSA demonstrated superior PFS, ORR, QoL, and symptoms relief with no significant difference in overall survival compared to carboplatin/paclitaxel in previously untreated patients, with locally advanced or metastatic NSCLC, whose tumours harboured activating mutations of the EGFR tyrosine kinase.

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