REGULATORY SUCCESS IN LABELLING HRQOL AND SYMPTOMS FOR NSCLC THERAPIES

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INTRODUCTION

- Patients with Non-Small Cell Lung Cancer (NSCLC) report symptoms (e.g. cough, chest pain, and shortness of breath) and poor Health-Related Quality of Life (HRQoL), particularly at advanced stages of the disease. Several patient reported outcomes (PRO) instruments are used in clinical trials to record patient experience.
- In light of increasing focus on patient-focused drug development, the EMA and the FDA have produced, and are continuing to update, guidance documents on the use of PRO to support label claims generally[1, 2,] and specifically in oncology[3].
- This review of regulatory labels for NSCLC therapies was conducted to better understand the landscape of PRO-based label claims, including symptoms and HRQoL.

METHODS

- A search in the PROLABELS™ database was performed for “Carcinoma, Non-Small-Cell Lung” in May 2019. Drugs approved with PRO-labeling claims from FDA and EMA were included, with no date restrictions.
- Label text from the corresponding agency website was reviewed for each identified record.
- The drug, trial design, concept measured, instrument, and endpoint were abstracted and summarized.

RESULTS

- The screening process identified 18 labels of which 2 records were excluded, 1 mentioning only performance status and 1 duplicate.
- From the 16 labels finally abstracted, 3 labels were from FDA and 13 from EMA, corresponding to 14 drugs, i.e. two drugs had labels in both agencies.
- For 10 drugs, PRO label claim was approved based on data from a single trial while for 4 drugs it was approved based on data from more than one trial.
- All PRO efficacy data came from Phase 3 randomized trials which primary endpoint was overall survival and/or progression-free survival; for 5 drugs, the trial design was open-label.
- Only for 4 trials was it specified that secondary outcomes included HRQoL and/or symptoms reported by the patient, and for 2 they were considered exploratory. For the rest, label text did not specify the level at which PRO endpoints were included within the testing hierarchy.
- EMA granted more HRQoL claims than the FDA. EMA included both HRQoL and symptom data for 10 out of 13 drugs and symptom data only for the remaining 3 drugs, while all FDA labels included only symptoms (3 out of 3) (Figure 1).
- Specific symptoms were mentioned in 9 labels. Symptoms most frequently included were: dyspnea, pain and cough. Other symptoms included fatigue, appetite loss, diarrhea, alopecia, hemoptysis, peripheral neuropathy, dysphagia and sore mouth (Figure 2).
- Three lung cancer-specific instruments were identified: EORTC QLQ-LC13, LCSS and FACT-L (used in 6, 5 and 2 labels, respectively) (Figure 3).
- General health status was reported using EORTC QLQ-C30 and EQ-5D (5 and 4 labels, respectively) (Figure 3).
- Four labels did not report the instrument used (Figure 3).
- Endpoints were: time to deterioration in 9 labels, change from baseline in 5 labels, and improvement rate in 3 labels (Figure 4).
- Timepoint for change from baseline was only specified in 2 labels, week 48 and 6 months.
- Threshold for deterioration was only reported for EORTC-QLQ-LC30 (≥10-point increase in scores from baseline) in 3 labels.
- In general, the EMA labels provided more details regarding PRO instruments and endpoints that were the basis for labeling.

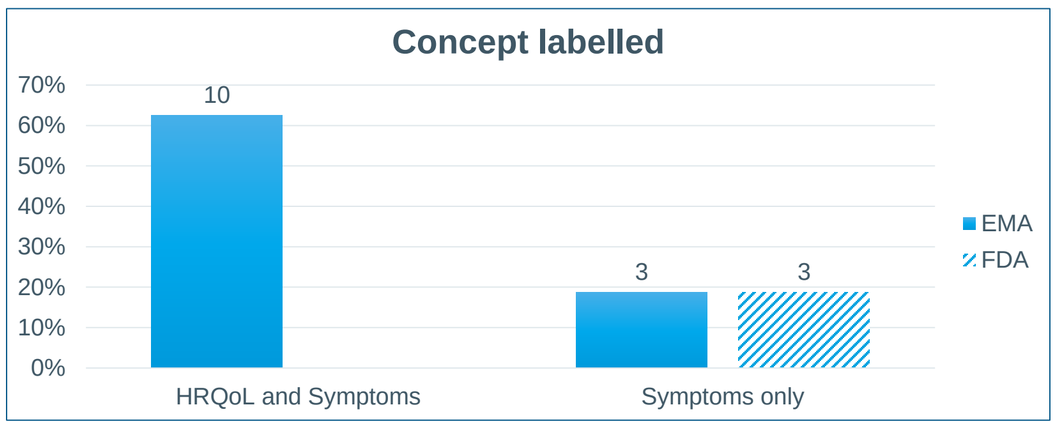

Figure 1. Concept labelled in the 16 labels abstracted by agency.

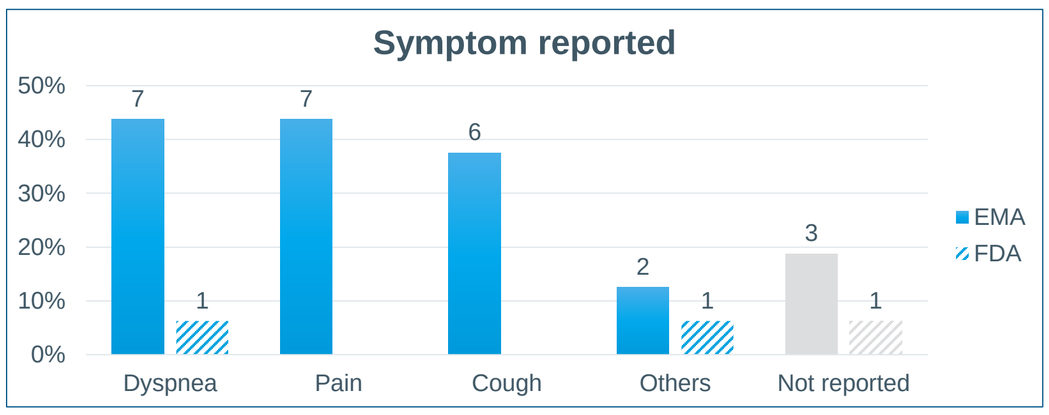

Figure 2. Symptom reported in the 16 labels abstracted by agency.

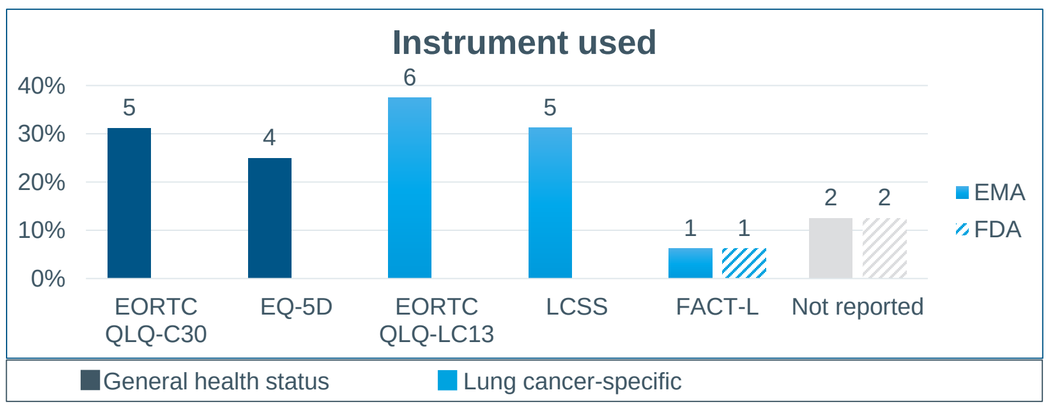

Figure 3. Instrument used in the 16 labels abstracted by agency.

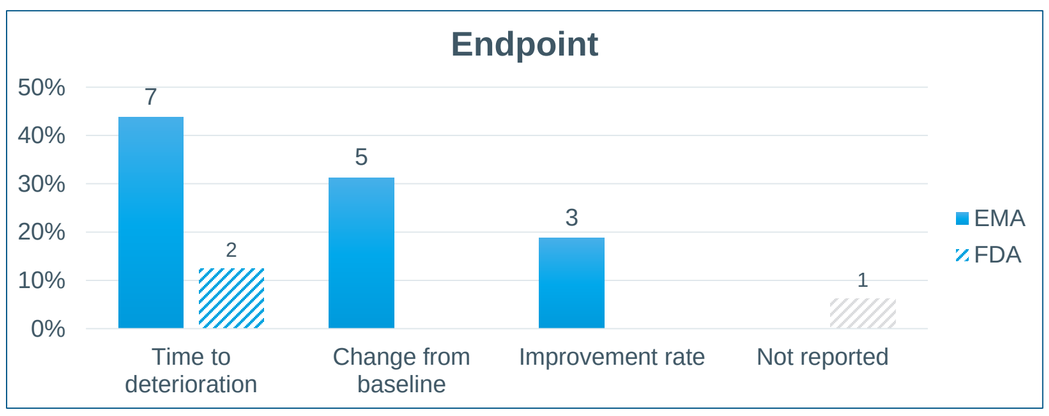

Figure 4. Endpoint in the 16 labels abstracted by agency.

CONCLUSIONS

NSCLC therapies that succeed in primary endpoints do not always result in PRO efficacy data to report in the label. Despite the increased interest of the FDA and the EMA in the patients’ perspective during the drug development and approval process, reflected by guidance from both agencies on PROs generally[1, 2] and in oncology[3], there are relatively few PRO claims included in packaging to date.

Our search showed that EMA and FDA have different standards regarding PRO data included in labelling and the claims are often limited and vague. This highlights the importance of a thorough development, validation, and implementation of PRO instruments, and close interaction with the regulatory authorities to obtain a targeted PRO label claim.

1. US Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (2009): Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims.
2. European Medicines Agency, Committee for Medicinal Products for Human Use (CHMP) (2005): Reflection Paper on the Regulatory Guidance for the Use of Health-Related Quality of Life (HRQL) Measures in the Evaluation of Medicinal Products.
3. European Medicines Agency, Committee for Medicinal Products for Human Use (CHMP) (2016): Appendix 2 to the guideline on the evaluation of anticancer medicinal products in man. The use of patient-reported outcome (PRO) measures in oncology studies.

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