

# Careful take-off by the EQ-5D-5L tool in lung cancer: fly little one, fly!

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Any stakeholder involved in lung cancer realises that preservation or improvement of health-related quality of life (HRQoL) is as relevant as the gain in life expectancy and the avoidance of complications. The quality-adjusted life years (QALY) concept combines the gained years and the change in HRQoL in one measure by correcting the former using the latter. Experts and decision-makers do request HRQoL assessments to be included in oncology trials. This goal is achieved in approximately 70% of trials.<sup>1</sup>

The EuroQoL 5-dimension 5-level (EQ-5D-5L) is a generic tool (besides others, eg, the EORTC Core Quality of Life Questionnaire (QLQ-C30) and FACT-G score) to measure health and HRQoL. It is generic as it can be applied to many disease entities with dimensions of health relevant for all. It was developed by EuroQoL (EQ) and measured 5 health dimensions (5D): mobility, self-care, daily activities, pain and anxiety. The patients' answers were on a 5-level scale (5L) map. One EQ visual analogue scale (EQ-VAS) is added as a 'thermometer' reflecting the persons' global health in one figure (range 0–100). Compared with other tools, the EQ-5D-5L is a small questionnaire. It has the advantage of a low questionnaire burden but inherently risks a low 'signal' resolution when used as a symptom monitor. This can of course be countered by adding 'tailored' symptom lists of interest. Depending on the geographical region, different 'single figure' health values (or utility scores) are attributed to the 3125 possible answer combinations of the EQ-5D-5L where 1 means perfect health and 0 is health as bad as dead.<sup>2</sup> Remarkably, some values go below 0, meaning the person scores health worse than death. Utility scores are available for other generic tools such as the QLQ-C30 (based on the QLU-C10D), although not all geographic regions are covered.<sup>3</sup> Sequential measurements allow to monitor the

effectivity of a therapy beyond gained life years. In addition, the coupling to utility scores allows economic evaluations.

In the article by Liao *et al*,<sup>4</sup> the prognostic value of the utility scores corresponding with the EQ-5D-5L answer patterns and of VAS scores was investigated retrospectively in 379 patients with lung cancer receiving first-line or second-line (chemo)immunotherapy. Besides, a list of patient-reported symptoms was tested for its prognostic value. There was one sequential evaluation of these potential prognostic factors 0.8 months later allowing the calculation of a mean difference versus baseline. The authors found that a lower EQ-5D-5L utility (HR 0.8, 95% CI 0.7 to 1.0) and a higher symptom burden (HR 1.1, 95% CI 1.0 to 1.2) at baseline had prognostic value as did the change in symptom burden (HR 1.1, 95% CI 1.0 to 1.2). The EQ-VAS had no prognostic value, in contrast with its change versus baseline.

The authors are to be commended as their work is innovative and of importance to the field of lung cancer. It is one if not the first in its kind to investigate the prognostic value of the utility score obtained by the EQ-5D-5L tool in patients with lung cancer receiving immunotherapy. Scarce (and mostly descriptive) data exist on the role of EQ-5D-5L for other lung cancer therapies, for example, thoracic surgery<sup>5</sup> or target therapy for driver mutations.<sup>6</sup>

The finding EQ-5D-5L as a generic tool may hold prognostic power on top of clinical and tumour characteristics (in particular PDL-1 expression) adds a piece to the puzzle on how to select patients who will benefit most from immunotherapy. The authors make a case in favour of electronic patient-reported outcomes (ePROMs) particularly for the EQ-5D-5L 'to guide real-world treatment decisions'. However, one swallow does not make a summer. So, these findings do currently not have direct implications for the clinic. In addition, cautious interpretation is



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warranted since this study is retrospective. The authors were confronted with a considerable fraction of missing data at baseline. Using a massive data imputation, the gaps were filled. The sample size was too small to investigate if the utility score could predict toxicity on immunotherapy in lung cancer, as was recognised by the authors. A bad utility score obtained by the EQ-5D-5L tool on its own is not capable of denying immunotherapy to patients.

The current report is at best a loud scream to widely test and validate the prognostic (and potentially predictive) value of the EQ-5D-5L tool in multivariate prediction models for survival, response and toxicity. Preferably, this is done in prospective data sets for different lung cancer therapies. Although the implementation of HRQoL tools outside trials is gaining terrain, it can be puzzling for stakeholders to make the right choices balancing between questionnaire burden, getting useful patient-reported data and information to guide treatment decisions. The comparison with other generic tools such as the QLQ-C30 would be informative. That could give the clinicians and researchers those handles needed to choose what fits best with the needs when implementing ePROMs such as EQ-5D-5L in routine practice.

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