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LETTER

Response Letter to "Letter: Cost-Effectiveness of Alectinib for Patients with Untreated ALK-Positive Non-Small Cell Lung Cancer in China"

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We really appreciate the great interest of Mu et al. in our research. As the choice of extrapolation model is very critical, we analyzed the influence of different parametric survival models on the results. Firstly, following a commonly used practical guide of extrapolation technique and model selection [1], we chose appropriate parametric survival models in our research on the basis of clinical rationality, visual fit, and statistical goodness-of-fit in the base-case analysis. Secondly, in another published economic evaluation of alectinib as first-line treatment, the most appropriate model was an exponential distribution for progression-free survival (PFS) and overall survival (OS) of both arms [2]; thus, this distribution was adopted to extrapolate the PFS and OS of two arms in scenario analysis. Thirdly, the Weibull distribution was also used for PFS in the alectinib arm in scenario analysis because of a slightly better statistical fit, even though it produced extended tailing that probably overestimated PFS after the 60th month. In addition, Cholesky matrix decomposition was conducted in probabilistic sensitivity analysis to further explore the uncertainty of parameters in the parametric survival model. Therefore, the results from long-term survival extrapolation have been fully considered in our research.

The clinical data used in our research was derived from the ALEX and ALESIA trials [3, 4]. The dose of alectinib in these trials was 600 mg twice daily, which is consistent with the recommended dose on the drug label approved in China, while the dose of alectinib in the J-ALEX trial was 300 mg twice daily [5]. Therefore, the J-ALEX trial should not be considered in our research. In addition, Mu et al. thought that there have been many published randomized controlled trials (RCTs) comparing ALK inhibitors with chemotherapy as first-line treatment for patients with ALK-positive non-small cell lung cancer (NSCLC). However, to our knowledge, for patients with untreated ALK-positive NSCLC, there were only three RCTs related to alectinib as first-line treatment, namely the ALEX, ALESIA, and J-ALEX trials, and the comparator in these three trials was crizotinib. Other clinical trials related to alectinib as first-line treatment for ALK-positive NSCLC were single-arm studies. Thus, we have considered all

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available clinical evidence related to alectinib as first-line treatment for ALK-positive NSCLC regardless of direct or indirect evidence.

We acknowledge that this analysis should be updated when new survival data is released and new clinical trials are conducted. In addition, the influence of the latest price of these ALK inhibitors through National Reimbursement Drug List negotiation should be further explored in the future.

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Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

Peer Review. Please note, contrary to the journal's standard single-blind peer-review process, as a letter, this article underwent review by a member of the journal's Editorial Board.

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