Peer Review File

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Reviewer A

A good paper. I think that studies like the above are of great importance in the current management of oncology costs and the consequent allocation of resources (Lancet Reg Health Eur 2021;3:100060). The same topic has already been addressed in the past by other Authors, again in reference to the costs of other TKIs in NSCLC and this can become a starting point for virtuous cost control with oncology drugs (Clin Lung Cancer 2016 Mar;17:91-94). This should be stressed in the text citing these papers.

Response: We have made detailed explanations of the following contents in the manuscript. The rising cost of newly registered oncology drugs poses a serious threat to the sustainability of national health service systems, particularly in countries with limited public control and cost oversight, such as the United States (41). This trend underscores the need for transparency and value-based pricing in the pharmaceutical industry.

To address this issue, pharmaceutical companies should disclose their research and development costs. Ensuring that the pricing of new treatments reflects not only their added benefits but also considers the societal and personal costs is crucial. This approach emphasizes the importance of a 'just price' that aligns with the true value of the treatments (41,42).

Reviewer B

1) Although the content of the report seems to be fairly straightforward, it is very similar to a previous report discussing QALYs with crizotinib in ROS1-positive NSCLC [BMC Cancer . 2021 Oct 29;21(1):1162. doi: 10.1186/s12885-021-08746-z.], and there is no discussion of the differences between the two reports.

Response: We have made detailed explanations of the following contents in the manuscript. Previous studies have shown that crizotinib is not cost-effective as a first-line treatment for ROS1+ NSCLC in Canada (41). Compared to our research on entrectinib in the United States, although entrectinib is not cost-effective in either the first- or second-line settings, the ICER for second-line treatment is relatively more favorable, being lower than that for first-line treatment ($1,090,594.30 vs. $494,290.39/QALY). This suggests that it could be considered as a compromise solution.

- Is there little scientific novelty to begin with?

As for the estimated administration costs and the costs of disease management cost, the authors need to be described. How it was calculated?

Response: We have made detailed explanations of the following contents in the manuscript. Administration costs in this manuscript refer to ward management and administrative expenses, which are only recorded once per cycle for treatments requiring intravenous medication administered in a hospital setting. As oral medications do not necessitate hospitalization, their associated expenses are not included in the administration costs. Disease management cost, which includes expenses pertaining to tumor imaging costs (computed tomography), and laboratory examinations cost, physician visit costs. Laboratory testing costs and physician visit costs were measured at a frequency of once per treatment cycle, whereas tumor imaging costs

were documented every two treatment cycles.

- Is there a maximum or minimum value?
- Should have been clearly stated? (Including specific amounts for each individual treatment)

Response: We have made detailed explanations of the following contents in the manuscript now: “the mean costs of entrectinib as a first-line treatment, second-line treatment, and chemotherapy were $113,738, $93,766, and $40,286 per patient, respectively. The corresponding QALYs for patients in these three arms were 0.44, 0.49, and 0.38, respectively.”