Review of: "TROPION-Lung01 Results Indicate PFS Benefit with Datopotamab Deruxtecan over Docetaxel in Previously Treated Nonsquamous NSCLC: A Critique and Question"

Laxman Subedi[1]

1 Deapartment of pharmacy, Mokpo National University, Korea, Republic of

Potential competing interests: No potential competing interests to declare.

The author has provided effective critical review comments on the topic “TROPION-Lung01 Results Indicate PFS Benefit with Datopotamab Deruxtecan over Docetaxel in Previously Treated Nonsquamous NSCLC: A Critique and Question,” which can be one of the insights for both clinicians and researchers. However, there needs to be clarification as well as some more addition of explanation based on various areas as mentioned below. Please revise the following contents:

1. Clarification of Study Objectives

The manuscript should clearly define the objectives of the commentary. While it appears the focus is on progression-free survival (PFS) and overall survival (OS), additional emphasis could be placed on how the results might alter clinical decision-making for NSCLC treatment. For example, explicitly address how these findings could influence treatment guidelines or the selection of patients for Datopotamab Deruxtecan (Dato-DXd) therapy.

2. Detailed Discussion on Absolute and Relative Risks

The commentary briefly mentions absolute and relative risks, but it would benefit from a deeper analysis. More elaboration on how the CONSORT guidelines apply to this study is needed. For instance, the authors could:

Include a table comparing absolute and relative risks between the Dato-DXd and docetaxel groups.

Explain the clinical relevance of these risk differences in terms of patient outcomes and treatment decisions.

Discuss the importance of communicating these risk metrics clearly to patients.

3. Addressing the Lack of Overall Survival (OS) Significance

The manuscript acknowledges that there was no significant improvement in OS, but this point deserves more critical examination. For example:

Why might there be a significant PFS benefit without a corresponding OS benefit? Are there underlying factors, such as treatment crossover or subsequent therapies, that might explain this?

How does the lack of OS benefit affect the clinical value of Dato-DXd? This should be contrasted with other available

therapies.

4. Addressing Spin in Study Results

The commentary poses the question of whether the TROPION-Lung01 study results include "spin," but this point is not sufficiently explored. For improvement:

Define what constitutes spin in clinical trial reporting (e.g., overemphasizing PFS when OS is the more clinically meaningful endpoint).

Critically assess whether the study authors appropriately balanced the presentation of PFS and OS results or if they exaggerated the PFS findings to downplay the lack of OS significance.

Offer recommendations for how future studies should present similar findings more transparently.

5. Greater Focus on the Squamous Subgroup

The findings related to the squamous histology group, which showed an increased risk of progression with Dato-DXd, are critical but understated in the commentary. A more detailed discussion should be included:

What are the potential biological or molecular reasons for the poorer outcomes in this subgroup?

How should oncologists approach the use of Dato-DXd in patients with squamous histology based on these results?

Are there alternative treatments that might be more suitable for squamous NSCLC?

6. Practical Guidance for Communicating Results to Patients

The manuscript highlights the importance of explaining complex clinical trial results to patients, but this section is underdeveloped. Suggestions for improvement include:

Provide a framework or example of how oncologists might explain the differences between PFS and OS in simple terms for a lay audience.

Address the ethical considerations of discussing treatments that show a PFS benefit without an OS benefit, particularly in terms of patient expectations and decision-making.

7. Incorporating Newer Literature and Broader Context

While the commentary references the TROPION-Lung01 study and other recent news reports, it would benefit from a broader contextualization of the findings within the current landscape of NSCLC treatments. For example:

How do these findings compare with other recent advancements in NSCLC treatment, such as immunotherapy or targeted therapies?

Are there other ongoing trials that may provide more clarity on the role of Dato-DXd in NSCLC?

8. Further Exploration of Safety Concerns

The manuscript briefly mentions the safety profile of Dato-DXd, but more in-depth analysis would strengthen the critique:

Explore the significance of the treatment-related interstitial lung disease/pneumonitis, especially in the context of long-term safety monitoring.

How do the safety outcomes compare to other second-line or third-line therapies for NSCLC?

9. Formatting and Structure

Improve the flow by clearly delineating sections such as "Risk Analysis," "Safety Profile," "Clinical Implications," and "Patient Communication."

The introduction could be more succinct, as the current version repeats some information already contained in the abstract. Consider consolidating these details to provide a clearer focus for the commentary.

10. Conclusion Strengthening

The conclusion needs more definitive recommendations. Rather than merely summarizing the results, offer clear takeaways for clinicians, such as when to consider Dato-DXd over other therapies and how to counsel patients on the likely outcomes.

By addressing these issues, the manuscript will provide a more comprehensive critique and offer valuable insights for both clinicians and researchers.

Response

Acceptance after the additional modification with the above-mentioned suggestions.