

Peer Review File

Article information: <https://dx.doi.org/10.21037/tlcr-23-200>

The authors have comprehensively summarized the latest findings on the role of first-line management of advanced non-small-cell lung cancer, rendering it an engaging topic. I have a few minor comments, explained below.

Reply: Thanks for this comment

Minor comments:

1. The significance of co-mutations, such as KEAP1/STK11, as critical factors in incorporating CTLA-4 antibodies should be addressed by the authors.

Reply 1: We agree and add a paragraph on the section of bi IO

2. Tumor burden, as an important predictive clinical factor in choosing between immunotherapy alone vs. immunotherapy plus chemotherapy, warrants the authors' commentary.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8902087/>

[https://www.ejca.com/article/S0959-8049\(21\)01220-X/fulltext](https://www.ejca.com/article/S0959-8049(21)01220-X/fulltext)

Reply 2: A low tumor burden, is probably a factor in favor for mono immunotherapy but there is a lack of prospective studies to confirm it. We add a sentence about this fact and also the 2 suggested ref.

3. The authors should include the ISNGINA Phase 3 trial (NCT03793179) in their discussion of immunotherapy alone vs. immunotherapy plus chemotherapy.

Reply 3: We agree and add it.

4. A Japanese study group is conducting a Phase 3 trial comparing platinum combination chemotherapy plus nivolumab and ipilimumab vs. chemotherapy plus pembrolizumab. This reviewer recommends citing this trial.

<https://www.sciencedirect.com/science/article/abs/pii/S1525730421002710>

Reply 4: We are not aware of this study. Thanks. We add it.